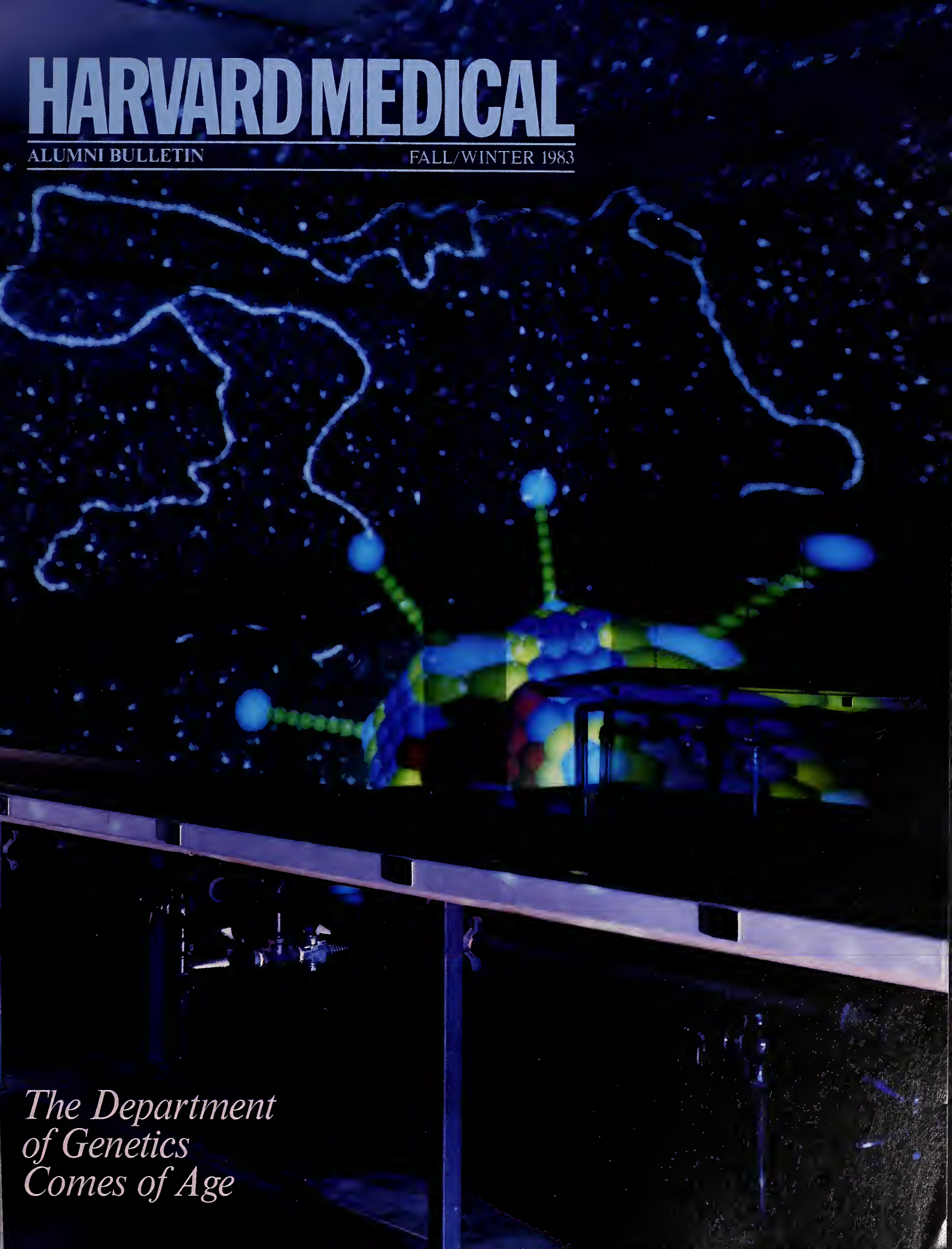
HARVARD MEDICAL

ALUMNI BULLETIN FALL/WINTER 1983



The Department of Genetics Comes of Age

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HARVARD MEDICAL

ALUMNI BULLETIN / FALL-WINTER 1983 / VOL. 57, NO. 4

FEATURES

DEPARTMENTS

Photographer Lorie Novak created the cover by projecting slides into a laboratory. The top of the image is an electron micrograph of a human gene and its mouse analog bonded together; the "bubbles" are the only places where they differ. Electron micrograph by Hunt Potter of the Department of Genetics. The colorful orb is a computer-generated model of the adenovirus molecule, commonly used in genetics and other research, courtesy of Richard J. Feldmann of the National Institutes of Health.

Note: *Two years ago, when the* Bulletin *changed its schedule and size, the first quarterly issue was unfortunately called Summer 1981—unfortunate because the Alumni Day/Class Day issue will always come out in time for fall, never for summer. With this issue (named Fall/Winter 1983, so you'll know you haven't missed a* Bulletin*) we have properly aligned our publication schedule with the seasons. The next issue you'll see will be Spring 1984, just in time for the very first buds.*

INSIDE H.M.A.B.

Mendel, thou should be living at this hour; Harvard has need of thee.

If this adaptation of Wordsworth's well-known lines seems ambiguous, then the balance of the quotation—"she is a fen of stagnant waters"—is totally inappropriate. The new Department of Genetics is anything but.

In this issue of the *Bulletin*, we seek out Philip Leder '60, professor and chairman of the school's newest, the Department of Genetics. Those of us who are comfortable in our world of garden peas and fruit flies are introduced to the brave new world of oncogenes and genetic engineering. And we become privy to the interaction of university and industry: Harvard Medical School with Du Pont, Massachusetts General Hospital and Howard Goodman with Hoechst.

We follow with two remarkable stories by Max Eddy '34. The stories were privately published by Barney Crile '33 for Max's friends. They were brought to our attention by Gordon Donaldson '35; now he and Max have gone—it is a fitting way to remember them both.

Tom Gutheil '67 returns to our pages with a lively treatment of the insanity defense and succeeds, where usually our legal colleagues fail, in making the subject intelligible. It does have a certain attraction for an editor. In a serious vein, Michael Stewart '65 reaches out to us in poems of self renewal and acceptance of new challenges that characterized his life so early ended. In Student Forum, Doreen O'Hara '83, formerly of our editorial board, recalls the formative period of a surgical clerkship and that hardy perennial, women in surgery. Finally, James Gordon '67 of the NIMH challenges us to think unemotionally about holistic health by taking us behind the name.

Blithely we move into the Medical School's third century with the hope that a troubled world is turning toward the morning. And, oh yes, changes are in the offing for the alumni as Perry Culver and Carl Walter step down after years of loyal service as director of alumni relations and chairman of the Harvard Medical Alumni Fund respectively.

—Gordon Scannell

HARVARD MEDICAL
ALUMNI BULLETIN

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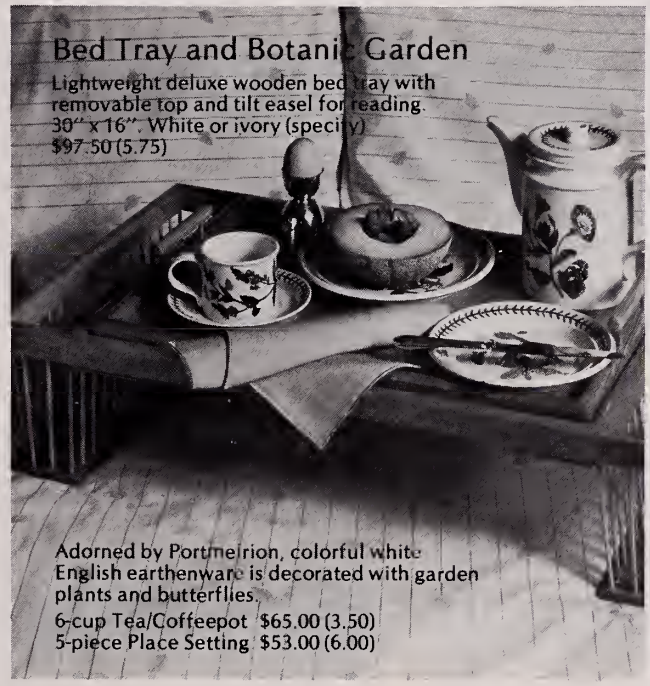

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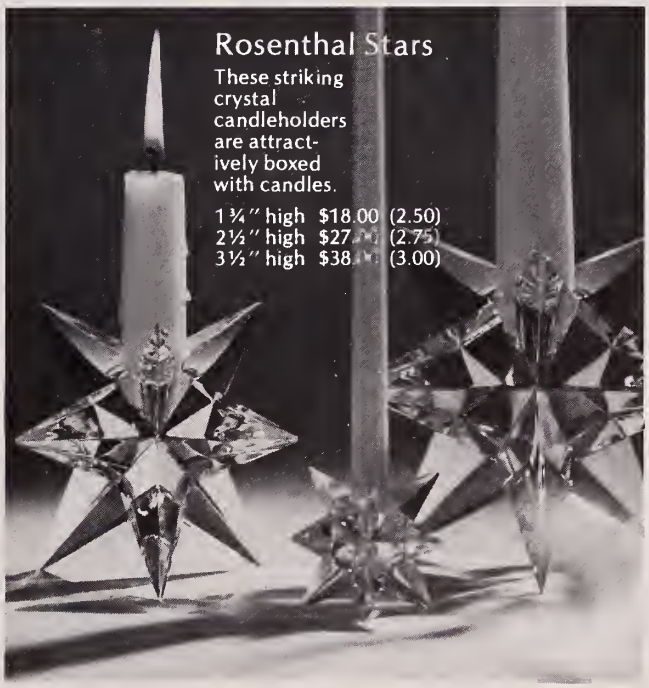

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Birth of a Building

While the echoes of pile driving faded away and a foundation was poured, construction of the Biosciences Research Building was officially inaugurated with a celebration of research at Boston's Musuem of Fine Arts on October 18.

The building, which Dean Tosteson called "a house for discoveries that will shape the medicine of the future," is a joint venture of Brigham and Women's Hospital, the Howard Hughes Medical Institute, and Harvard Medical School. "Bringing great institutions nearer to each other," Tosteson said at the inauguration, "is like getting porcupines to mate." Somehow, any prickly barriers were surmounted, and the union was achieved.

The 15-story Biosciences Research Building will stand directly across Shattuck Street from the Laboratory of Human Reproduction and Reproductive Biology (LHRRB). A bridge spanning Shattuck Street will connect the sixth floor of LHRRB to the fourth floor of the new structure. Four floors of the building will house the branch of HMS's Department of Genetics located in the medical area. (The other major component of the department is at Massachusetts General Hospital, and will eventually occupy four floors of the Wellman Research Building, also under construction. See "Genetics: The Youngest Basic Science," page 16.) Eight and one-half floors will be occupied by the Brigham and Women's Hospital departments of Surgery, Medicine, Pathology, Orthopedics, Anesthesiology, and Radiology. Hughes Institute scientists will use the remaining floors.

During the inauguration, teams of scientists from the three institutions presented recent advances in their fields. Eugene Braunwald and Thomas Smith '65 from Brigham and Women's Hospital gave an overview of developments in cardiovascular disease; George Cahill and William Chin '72 of the Hughes Institute described studies on the genes for hormones that regulate reproductive function; Philip Leder '60, chairman of the HMS Department of Genetics, and Jonathan Seidman, assistant professor of genetics, discussed work on the genetics of organ transplantation.

In his welcoming remarks, George Thorn, president of the Hughes Institute, described the institute's support of research in genetics, immunology, metabolic regulation, and neurosciences in association with 10 medical schools. He also commented that he was qualified to represent all three participants in the new building: for

S. James Adelstein '53, dean for academic programs; Francis D. Moore '39, Moseley Professor of Surgery emeritus; George Hitchings, president of the Burroughs Wellcome Fund; and Joseph E. Murray '43B, professor of surgery at Brigham and Women's Hospital. The Burroughs Wellcome Fund has contributed to a Transplantation Biology Laboratory in honor of Drs. Hitchings and Murray: in the early 1950s Hitchings developed the immunosuppressant drug Murray used to prevent rejection in the first successful kidney transplant.

H. Richard Nesson, president of Brigham and Women's Hospital.

Thomas W. Smith '65 and Eugene Braunwald, both of Brigham and Women's Hospital, at their presentation on cardiovascular research.

George Thorn, president of the Howard Hughes Medical Institute, with Dean Tosteson.

Jonathan Seidman, assistant professor of genetics, and Philip Leder '60, chairman of the Department of Genetics.

George F. Cahill, Jr., professor of medicine at HMS and director of research at the Hughes Institute, with William W. Chin '72, assistant professor of medicine at HMS and associate investigator at the Hughes Institute.

30 years he was chief of medicine at Peter Bent Brigham Hospital and Hersey Professor of the Theory and Practice of Physic at HMS.

"This building," said H. Richard Nesson, president of Brigham and Women's Hospital, "is testimony to the priority that research has at Brigham and Women's Hospital, Harvard Medical School, and Howard Hughes Institute. I have great faith that the contributions that will result will be of value to all society."

In his after-dinner speech, Francis D. Moore '39, Moseley Professor of Surgery emeritus and for 28 years chief of surgery at the Brigham, likened research to peeling an onion. "You're ignorant at the start, you take off the layers, and you find it more and more concentrated, a denser and denser node of ignorance. And all the time you're weeping about how much it costs to get there." Nationally, "nowhere near enough" money is devoted to research, he emphasized, quoting an investigator who said: "There never was a scientist whose work was so basic that he didn't in his dreams conceive of how it might help mankind."

"We're here to celebrate a human activity, not just a bunch of buildings," Dr. Moore summarized. "These laboratories will add structure to the edifice of knowledge, and give young people the opportunities that will lead to victories" in the conquest of illness.

A Decade of Leaders

This year, the Leaders in American Medicine series marks its 10th season. Since its founding in 1974 by George E. Gifford, Jr., the series has annually presented films and discussions celebrating a few distinguished physicians. So far, the 1983-84 season has seen programs on Tinsley R. Harrison and Oliver Cope '28. Francis C. Wood, Mark D. Altschule '32, and Paul I. Yakovlev will be honored in the coming months.

The next session, scheduled for February 1, will feature Francis C. Wood, Frank Wister Thomas Professor of Medicine emeritus, University of Pennsylvania. Chairman of the Department of Medicine at the University of Pennsylvania School of Medicine from 1946 to 1964, Dr. Wood has long been recognized for his outstanding teaching. He was part of the team that worked out the optimal placement of precordial leads for the electrocardiogram.

Participants in this session will be Russell S. Boles, Jr., senior physician, New England Baptist Hospital; John T. Potts, Jr., Jackson Professor of Clinical Medicine, HMS; and Truman G. Schnable, Jr., C. Mahlon Kline Professor of Medicine, University of Pennsylvania.

Mark D. Altschule, former clinical professor of medicine, HMS, and co-author with Dr. Henry K. Beecher of *Medicine at Harvard, The First 300 Years,* will be featured on March 14. Altschule, a former president of the Boston Medical Library, will be joined by Norman Geschwind, James Jackson Putnam Professor of Neurology, HMS; Howard A. Frank, clinical professor of surgery, HMS; and Stewart Wolf, professor of medicine, Temple University.

This season's final program, which will take place on April 18, will be devoted to the late Paul I. Yakovlev, clinical professor of neuropathology emeritus, HMS. Dr. Yakovlev's research discoveries became the basis for stereotaxic brain operations, a type of procedure used to treat Parkinson's and other diseases by eliminating the small areas of the brain that cause abnormal movements. Dr. Yakovlev made his findings by collecting and mounting on slides samples from the brains and spinal cords of more than 750 individuals; his collection has become a valuable research resource for people all over the world.

The discussants for the program will be Thomas L. Kemper, lecturer on neuropathology, HMS; Marjorie J. LeMay, associate professor of radiology, HMS; and Jerome Y. Lettvin, professor of communications physiology, MIT.

The late Tinsley R. Harrison, former professor of medicine, University of Alabama Medical School, was honored in this season's first program, held October 5. Dr. Harrison was the first editor-in-chief of the classic text *Principles of Internal Medicine,* and the founder of three departments of medicine. He was a seventh-generation physician who believed that medical education should be "much more a matter of the heart than of the mind." He was the recipient of the Kober Medal in 1968, and was Distinguished Professor of Medicine, the Veteran's Administration.

Discussants for this session were Raymond D. Adams, Bullard Professor of Neuropathology emeritus, HMS; Mark D. Altschule; and James A. Pittman, Jr., dean, University of Alabama School of Medicine.

The second session of this series, held November 9, was devoted to the past and continuing achievements of Oliver Cope, senior surgeon, Massachusetts General Hospital, and professor of surgery emeritus, HMS. Dr. Cope is perhaps best known for having developed burn treatments used after the Cocoanut Grove fire and during World War II, and for his pioneer surgical treatment of disorders of the parathyroid glands. His book *The Breast* challenged the procedure of mastectomy in favor of less radical surgery.

Participants in the program included Farahe Maloof, professor of medicine, and Earle W. Wilkins, Jr., clinical professor of surgery, both at HMS.

Leaders in American Medicine is run under the auspices of Dr. Leroy D. Vandam, Mark D. Altschule, Dr. J. Worth Estes, Richard J. Wolfe, and Mrs. George E. Gifford, Jr. The series is sponsored by Boston University School of Medicine, Benjamin Waterhouse Medical History Society, Boston Medical Library, Brown University Program in Medicine, HMS, and Tufts University School of Medicine. It is made possible by grants from Smith, Kline and French Laboratories and the Josiah Macy, Jr., Foundation.

All sessions are held on Wednesday afternoons at 4:30 in the Countway Library; refreshments are served a half-hour before each program commences.

Foster's First Freshmen

"They're in for a treat when they get to know each other," said Gerald Foster '51 this September as he surveyed the entering Class of '87, the first selected since he became director of admissions.

Although, in keeping with the national trend of decreasing applications, fewer people applied (3,222 this year, 3,573 last year), many more applicants were interviewed: 998 HMS applicants, and 115 Health Sciences and Technology (HST) applicants, as opposed to 814 and 114 last year.

The 165 students selected with such care represent 32 states, Puerto Rico, Canada, and Hong Kong. As always, New York supplied the most matriculants (31), followed by Massachusetts (23), California (21), Pennsylvania (15), and New Jersey (10).

Entering students come from 65 colleges, from Adelphi to Xavier, the highest number, as always, coming from Harvard/Radcliffe (37), followed by Yale (11), MIT (8), Princeton (8), and Stanford (6). Brown and Cornell each contributed five matriculants, UC San Diego and the University of Pennsylvania each four, and Brandeis, UC Berkeley, University of Chicago, Dartmouth, Middlebury College, and Williams College three apiece.

Foster's conviction that older students "bring an extra dimension of experience and ability" is reflected in the age range of the class (from 18 to 34) and in the higher number of

Message to the Alumni from the President of the Alumni Council

The Alumni Council is confronted with an unusual problem. The terms of office of the Director of Alumni Relations and the Chairman of the Alumni Fund are up for review as of June 30,1984, and both Perry Culver '41 and Carl Walter '32 feel the time has come for the younger generations to assume responsibility. They have therefore asked to be relieved of their respective positions as of June 30, 1984.

It will be difficult, if not impossible, to find two such gifted, energetic, and capable alumni for these positions. It is, however, the constitutional responsibility of the Harvard Medical Alumni Council to do so to the best of its ability.

As mandated by the constitution, two committees have been formed to review the job descriptions and to activate the selection process. Grant Rodkey '43A is chairman of the Nominating Committee for the Director of Alumni Relations. Robert Lawrence '64 is chairman of the Nominating Committee for the Chairman of the Alumni Fund. We encourage all alumni to submit any ideas or names to Drs. Rodkey and Lawrence through the Harvard Medical Alumni Office.

More detailed information will be published in a future issue of the *Bulletin.*

Joseph E. Murray

Joseph E. Murray '43B

students 25 and older (26 this year; 20 last year). Six applicants took advantage of Foster's new liberalized policy of deferred admission to spend this year on a project that will be personally or intellectually rewarding, and are expected to matriculate next year.

Though the number of science majors (123) is lower and the number of social science and humanities majors (32) is higher than last year, both the science and the non-science grade point averages are even higher than those of last year's entering class. MCAT scores are also up slightly, averaging 11.37. Humanities majors apparently were highly attractive candidates, forming 7.29 percent of applicants but 10.9 percent of entering students.

The class includes 26 minority students, 10 alumni offspring, and 58 women, the third highest number of women ever in an HMS class. It also includes a Rhodes scholar, two Marshall scholars, and three Peace Corps veterans. And next year's second-year show already promises to be a humdinger since, along with many other talented individuals, the class includes a graduate of Ringling Brothers Barnum & Bailey Clown College.

The Class of 1987

Aisenberg, James
Boston, MA (Harvard)

Alter, Craig A.
Valley Stream, NY (U. of Pennsylvania)

Anderson, Susan E.
Wellesley, MA (Williams College)

Aragon, Thomas J.
San Francisco, CA (UC Berkeley)

Arbiser, Jack L.
Decatur, GA (Emory)

Bach, David L.
Minneapolis, MN (Harvard)

Backer, Jonathan M.
Waban, MA (Harvard)

Baker, Elissa M.
Brookline, MA (Brown)

Baker, James H.
Mt. Vernon, AL (U. of Alabama)

Barncastle, John P.
Albuquerque, NM (U. of New Mexico)

Becker, Anne E.
Whitefish Bay, WI (Harvard)

Born, Richard T.
Wauwatosa, WI (DePauw)

Brodey, Benjamin B.
Oslo, Norway (MIT)

Buchthal, Rebecca H.
Scarsdale, NY (Middlebury College)

Budenz, Donald L.
New Britain, PA (U. of Pennsylvania)

Burack, Jeffrey H.
Mount Royal, Quebec (Harvard)

Bures, Joanna
Bogota, NJ (Cornell)

Burley, Stephen K.
London, Ontario, Canada
(U. of Western Ontario)

Calcagno, Jeffrey L.
Cos Cob, CT (Harvard)

Campbell, Crawford C.
Centre Harbor, NH (U. of Utah)

Campion, Francis X.
Watertown, CT (Holy Cross)

Campo, Stephen L.
Winchester, MA (Harvard)

Carrazana, Enrique J.
Miami, FL (Georgetown)

Chaffey, Margaret H.
Downey, CA (Harvard)

Chen, Chinfei
Rego Park, NY (U. of Pennsylvania)

Chen, Neil T.
Rosemont, NY (Haverford)

Cherry, Sabrina
Tenafly, NJ (Brown)

Cigarroa, Carlos G.
Laredo, TX (Notre Dame)

Cohen, Evelyn T.
Potomac, MD (U. of Virginia)

Conigliaro, Joseph
Brooklyn, NY (NYU)

Cooper, Paul A.
Rockville, MD (Yale)

Costanzo, Joseph P.
Bronx, NY (NYU)

Cryns, Vincent L.
Lockport, NY (Harvard)

Cummings, David E.
Westfield, NJ (Dartmouth)

Curhan, Sharon E.G.
Great Neck, NY (Brown)

Diamandis, Peter H.
Kings Point, NY (MIT)

Dorfman, Andrew J.D.
New York, NY (UC San Diego)

Dressen, Elizabeth B.
Arlington, VA (Boston U.)

Dudley, Lorraine E.
Sudbury, MA (Princeton)

Dunn, Jocelyn J.
Walnut Creek, CA (Stanford)

Ellman, Matthew S.
Newton, MA (Cornell)

Ely, Elissa A.
Stamford, CT (Wesleyan)

Escribano, Rafael A., Jr.
Torrance, CA (U. of Washington)

Fingold, Diane R.
Framingham, MA (U-Mass Amherst)

Fox, Ellen E.
Malden, MA (Yale)

Fradd, R. Brandon
Gainesville, FL (Princeton)

Frank, Carolyn S.
Shaker Heights, OH (Harvard)

Fulop, Michael A.
Bronx, NY (Princeton)

Fung, Claire Y-K
Happy Valley, Hong Kong (Yale)

Garcia, Jose C.
Skidmore, TX (U. of Texas at Austin)

Garcia, Richard L.
Los Angeles, CA (UC Santa Cruz)

Gittes, George K.
La Jolla, CA (Harvard)

Glassman, Robert H.
West Haven, CT (Harvard)

Gliklich, Richard E.
Edison, NJ (Yale)

Gourevitch, Marc N.
Middletown, CT (Harvard)

Grajalea, Benjamin
Worcester, MA (Adelphi)

Grayson, Galen
San Leandro, CA (Morehouse College)

Greco, Peter J.
Westlake, OH (Harvard)

Greenberg, Jane A.
Baltimore, MD (Yale)

Gurley, Rita J.
Calhoun, GA (Emory)

Guyton, Thomas S.
Jackson, MI (U. of Mississippi)

Hampton, Jacqueline
Bronx, NY (Cornell)

Herman, Gary A.
Woodland Hills, CA (UC San Diego)

Hiehle, John F., Jr.
Wyomissing, PA (Cornell)

Hillegass, William B., Jr.
Clemmons, NC (Yale)

Ho, John P.
Cambridge, MA (Harvard)

Ho, Kalon K.L.
Loma Linda, CA (UC San Diego)

Hodgkinson, Martha M.
Buchanan, NY (Dartmouth)

Huang, Philip L.
New York, NY (Columbia)

Iralu, Jonathan V.
Malvern, PA (Yale)

Jacobs, Deborah S.
New Bedford, MA (Harvard)

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Jamaica, NY (Pace)

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Rochelle, IL
(U. of Illinois at Urbana-Champaign)

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Modesto, CA (Stanford)

Le, Khoi M.
South Bend, IN (Harvard)

Lee, Frank S.
St. James, NY (Harvard)

Leeman, Eve
Newton, MA (Harvard)

Leichter, Rhoda F.
Jamaica, NY (Harvard)

Lengyel, Carole A.
Woodbridge, CT (Harvard)

Leonard, Garrick H.
New York, NY (Williams)

Libby, Eric D.
Orinda, CA (UC Berkeley)

Lin, Paul P-Y.
West Chester, PA (Harvard)

Little, Julia E.
St. Albans, WV
(Virginia Polytechnic Institute)

Liu, Paul Y.
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Locke, Giles R.
Decatur, IL (DePauw)

Marcantonio, Edward R.
Abington, PA (Harvard)

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Carbondale, PA (U. of Pennsylvania)

Massaro, Anthony F.
Stoneham, MA (Boston College)

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Buffalo, NY (Carleton College)

McCue, Michael P.
Caldwell, ID (MIT)

McDonald, Janice A.
Columbia, SC (Vassar College)

McNamara, Dennis M.
Upper St. Claire, PA (Yale)

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Topeka, KS (Middlebury College)

Milheim, Stephen G.
Warren, OH (Amherst)

Mohrbacher, Ann F.
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Irwin, PA (Allegheny College)

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Howard Beach, NY (MIT)

Reyes, Caroline
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Wood, Paul A.
Mamaroneck, NY (Brown)

Wu, Wilson C-S.
Los Angeles, CA (UCLA)

Yook, Inkyung
Ridgewood, NJ (Smith College)

Who's on the Cover?

The members of the Class of '33 who appeared on the cover of the Summer '83 *Bulletin* are (left to right):

Top row: Joseph S. Lichty, Carter R. Rowe.

Third row: Mrs. Hunter, Max R. Hunter, Bradford Cannon, Kendall Emerson, Jr.

Second row: Carlton R. Souders, Robert A. Youngman, Mrs. Wheatley, George M. Wheatley, Merritt B. Low.

Seated: Mrs. Hyder, Prentiss Hyder, Mrs. Ingraham, Hollis S. Ingraham.

Correction: A Pulse item in the Summer '83 issue contained an error: a total of 1,800 (not 18,000) people attended the regional Bicentennial events.

STUDENT FORUM

You Ought to Be in Surgery

by Dorene O'Hara

When Dorene O'Hara '83 told the Bulletin *shortly before she graduated that she was working on a novel about her experiences in medical school, it was not much of a surprise to the staff. A prolific and valuable former member of the editorial board, she had contributed extensively to the* Bulletin *and to* The Present Illness, *a student publication. In these pages she has written on the premed syndrome, reviewed* The Making of a Woman Surgeon, *by Elizabeth Morgan, and evoked her experience in Vanderbilt Hall.*

In the following excerpt from her novel, O'Hara explores her introduction to surgery, and her burgeoning fascination with the field. Because the book is a fictional treatment of her HMS years, names have been changed.

Dr. O'Hara is now a surgical intern at McGaw Medical Center, Northwestern University, Chicago.

The first day of my two-month surgery clerkship, or clinical rotation, I arrived at the New England Deaconess Hospital at eight in the morning—bright and early, I thought. Then I found that the surgeons had been there for two hours already. From then on I would arrive when they did.

I was one of about 10 students, some of them third-year like me, some of them in their last year. We were to admit patients to the hospital under the supervision of a surgical resident, assist in the operating room, and take call when our residents did. There would be one other student at this hospital; the rest would work at other hospitals in the Deaconess system. We would work on our own, not in groups. I liked the idea of one-on-one teaching.

Surgery was my first rotation. In January of that year I'd taken a course in surgical techniques, and done a few operations on dogs under anesthesia. The instructor had commented on my dexterity, and I had found I liked operating.

One of my most traumatic days in the first year was in physiology lab. I vowed then I'd overcome my fear of surgery if it was the last thing I'd do.

It was a fairly new enthusiasm. One of my most traumatic days in the first year had been physiology "dog lab." Dr. Rodgers, in charge of the lab, had prepared us in advance, explaining that we would perform an operation on a dog, monitoring blood pressure and heart rate to see the heart's response to various drugs.

He had shown us a film which demonstrated the surgical techniques we would be using. I wasn't used to the sight of blood. I felt sick to my stomach—and this was just a film. All week long before the lab I was nervous. I was afraid to pick up a scalpel, and afraid I would faint in the middle of the experiment.

A few students—five or ten out of 160—felt the lab was a needless killing of an animal and refused to participate. I wasn't so sure about that, because I had done animal experimentation before and knew *that* was necessary and worthwhile.

These students argued that what we were doing had been done hundreds of times before, and that, unlike original research, this exercise would not demonstrate anything medical science didn't know already. It was solely an educational exercise for our benefit. And in a sense they were right. Our little dog lab wouldn't make anyone in Stockholm blink an eye.

But I disagreed, and so did most of my classmates, that the experiment was a waste of time. It was designed to teach *us* something new, something we couldn't read in a book. We would be demonstrating basic cardiac physiology in a live animal, and gaining an understanding that could not be duplicated by reading.

It was a chance to begin to work with our hands—to use scalpels and suture, to inject drugs. It seemed to me that if I had to choose between learning basic surgical techniques on animals or patients, I'd rather learn on animals.

Lab day arrived. When I warned my partner he might have to catch me when we started cutting, he predicted, "Don't worry, you'll be a star. I can just tell. You're a budding surgeon already."

"You must be kidding," I said. "Me, a surgeon? I'll be shaking like a leaf."

I thought back to the years when I'd dreamed of going to medical school. There was something awe-

inspiring about surgery, I had thought. One needed to be either God or Michelangelo to do it justice. I couldn't imagine then that I might have the technical ability to be a surgeon.

The dogs were already asleep under anesthesia when we arrived. Our lab instructor took us through the operation. We had to place a tube in one of the arteries leading to the kidney, to measure its blood flow. My partner started, then handed the scalpel to me.

"What are you giving me that for?" I asked. "You're doing just fine."

"Come on. You can't be shy forever. Get in there and CUT."

My hands shaking, I nicked the skin. The lab instructor looked over my shoulder. "What kind of incision is that? You're just brushing the hairs around."

I cut deeper. "Good. Now slip the tube in." I was shaking so much I missed the opening the first time. Finally I got it, and tied it into place. I wanted to die of embarrassment at my clumsiness, and I vowed I'd overcome my fear of surgery if it was the last thing I'd do.

Now it was the first day of my surgery clerkship, and because I had already missed rounds, the chief resident, Don Meyers, and I scrubbed in and went right into the operating room. It was brightly lit with blinding white lights reflecting everywhere off the immaculate chrome and glass. The operation was a kidney transplant. Dr. Tanner, head of the transplant service, was bending over the field as he prepared the patient to receive the organ. In the next room, his partner was removing the donor kidney from the patient's sister.

Dr. Tanner looked up and smiled at me with his eyes. "Here. Let me tell you what we're doing," he said. He showed me where the kidney would go—not in the back of the abdomen where it normally is, but just under the skin. The tiny blood vessels and ureters would be sewn with thread I could barely see.

Dr. Tanner let the third-year resident take over suturing for awhile. He watched over him like a hawk, loudly correcting him. "No, not like that!" he yelled. "Gently! Gently! That's a ureter you're mucking around with!" I couldn't believe the guy wasn't folding under the pressure. He just kept on going.

Dr. Tanner gave me some retractors to hold back the skin as he and the resident put the kidney in place. I grew tired from the constant pulling. Every time I let up, Dr. Tanner repositioned my hands and told me to pull harder. Don started kidding me: "What's the matter? Your first day and you can't hack a couple of retractors?"

I knew they would be watching me all the time, to see how I would hold up—especially because I was a woman, the only woman on the surgical service that month. "Don't worry about me," I said. "I'll hold these things all day if you want."

I found myself running all the time. The faster I got my work done in the evening, the faster I could get to sleep.

"Looks like we've got a tough cookie here, Don. Better watch out," Dr. Tanner said. He winked at me.

After we closed up, Don and I met in the surgeon's lounge. I looked at my watch. It was three in the afternoon. I had been in there for five hours. Suddenly I was hungry. "Aren't you going to eat anything?" I asked.

"What's the matter?" he asked. "Can't you skip a meal without fainting? You'd better get used to it in surgery."

I was going to have to get used to a lot of kidding around if I was going to make it. "Ok, ok, I'll be macho like you," I said. "I'll stay up all night and stop eating. Starting tomorrow. But right now we have nothing to do and I'm *hungry*."

He let out an exaggerated sigh. "Ok, Dr. O'Hara, looks like I'll have to baby you all month. Let's go eat." I smiled at him. Yes, he and I were going to get along just fine.

Every day I was responsible for admitting one patient scheduled for surgery the following day. My first was a woman admitted for a resection of a newly discovered cancer of the bowel. She was only 50; the cancer had been picked up on routine checkup by her doctor.

I tried to make my exam a fast one. It would be a long day for her, and the surgery was the next day. I asked her about past medical problems, taking notes, and did a full exam. She had no heart or lung disease that would pose any special problems in surgery. I put on a glove and felt the hard rectal mass. We talked a little then about the surgery. As I stood to leave, she grabbed my hand. "How bad is it?" she asked. "Please tell me."

I didn't know what to say. I sat on the bed, holding her hand. "You know you have a tumor in your bowel, right?"

"Yes."

"Well, it seems to be fairly small—we'll know more after the surgery—and it was picked up early. There's a very good chance for a cure."

I couldn't say much more. I didn't know enough. She seemed satisfied, but I advised her to talk to her doctor more about it when he came by that evening. I left to write up my exam, wondering why cancer happens, and when I would stop feeling awkward talking to patients about it.

The next morning I arrived at six, prepared with fresh clothes and a toothbrush, knowing I wouldn't return home again until the evening of the following day. I went on rounds with Don, trying to keep up with his fast-paced stride down the halls.

Very soon I learned why we had to do all that running around. There was barely enough time to see patients from 6:30 to 7:30 after group rounds, and, if we hurried, there would be time to hit the cafeteria for breakfast before scrubbing in. Otherwise, we would go without food until late afternoon or dinnertime. In fact, I found myself running all the time. The faster I got my work done in the evening, the faster I could get to sleep. Soon I was naturally moving as fast as the rest of them.

On rounds that morning we saw Mr. Amore, the patient who had had the kidney transplant. He wasn't doing so well. His kidney had stopped functioning, gradually dropping off from

minimal output to nothing in the past few hours.

Late in the afternoon we were back in the operating room. Don and Dr. Tanner found the problem: the ureter had slipped out so that urine was running into the abdomen instead of out. The kidney itself was working fine. They sewed the ureter securely into place. As we closed, Don looked up at me and asked,"Do you know how to tie?"

"I sure do," I said. I had been practicing my square knots at home nightly in preparation for the clerkship. My roommate thought I was crazy. I had bought a needle holder and sutures, and had tied black silk sutures in hundreds of knots. When the offer came, I knew it was my big chance. If I hesitated they might not offer again for weeks. I took the needle and thread, and started to put in the skin stitches.

Everyone gathered around to watch the new female medical student sew. I looked up to see about 10 pairs of eyes staring at me, and started to shake from nervousness. Inside, I was cursing myself. You idiot, I thought, you're getting nervous over nothing. You've done this plenty of times before in dog surgery. I finally finished, to my relief. Don pulled out a loose stitch and replaced it. We were done. "Good job," he said. Next time, I thought, I won't be so nervous. I did it once, I can do it again.

That week I did a lot of sewing. The residents liked me and saw that I worked hard, and the senior surgeons began to trust me. They would find me in the hallway and stop what they were doing to teach me a fact or two. They demonstrated important techniques and anatomical landmarks during the operations. They would scrub out at the end of the case saying, "You can let Dorene close up."

By the third or fourth case I wasn't nervous anymore. I sewed quickly and confidently. I cut hundreds of sutures, learned to use the cautery on small bleeders, and a few times was given the scalpel to make a cut or two.

During the cases, Don asked me anatomy questions to pass the time. After the first day, I realized that things would go much better if I was prepared. So I studied anatomy every day, getting the list of operations in advance so I could concentrate on what we'd be doing. Don would point to something and I would identify it. Nerves, muscles, arteries—I never missed any because I had just studied them. So then they would ask me harder questions: lists of the branches of arteries or nerves, the blood and nerve supply to certain muscles. I answered them all.

"Where did you teach anatomy?" one of the senior surgeons asked me.

I smiled. "No, really, I just studied, that's all," I said.

"Studying or not, you have a good memory and a good eye. You ought to be a surgeon."

I was seriously considering it. I

Ether Prints Available

October 16 marked the 137th anniversary of the first public demonstration of the use of ether in surgery. Supplied by Boston dentist William Thomas Green Morton, the ether was used to anesthetize Gilbert Abbott, a 20-year-old house painter, as Harvard surgeon John Collins Warren removed a tumor from his neck.

Artist Robert Hinckley painted the historic scene about 40 years later, using artistic license to add a few figures who were not actually present at the surgery in 1846. The painting is now owned by the Boston Medical Library, and displayed in the lobby of Countway Library.

Excellent color reproductions, 10½ by 12½ inches, fully matted, are now available for $15 each, postage included. Order from: Ether Print, Countway Library, 10 Shattuck St., Boston, MA 02115—or stop by Room 512.

found myself liking surgery more and more. I saw that it was not so mysterious after all, that it required dedication and a certain amount of skill—and a lot of hard work. I was reading about surgical problems, and getting involved with the patients' care. I wanted to learn how a surgeon thinks, and how to make a surgical diagnosis.

I met Dr. Sumner, an otolaryngologist, and his two partners. Since Don was going into plastic surgery and had a special interest in head and neck surgery, I found myself scrubbing in on these cases with him. I studied the complicated head and neck anatomy like crazy, memorizing the maze of nerves, arteries, and muscles, and assisting on the precise dissections in the face for tumor removal.

I couldn't do much, for this surgery was too delicate. Instead I tried to watch the surgeons' technique, seeing how they stabilized their hands so they could move the scalpel or scissors only millimeters at a time. Occasionally Dr. Sumner would let me cut some tissue or put in a stitch.

That month I also saw many other patients besides those with facial tumors. There was a 50-year-old man, a dentist, with rectal cancer. There was a woman with end-stage breast cancer, given higher and higher doses of morphine. There were diabetics with gangrene who needed amputations.

There was a young man, my age, just diagnosed as having Hodgkin's disease. Sure, we could tell him the disease was picked up early, and that chances for cure were good. With radiation and chemotherapy, he would live. But no matter what we said, it was very hard news for a young college track star to take. He spent a week on our service, and I talked with him every day. How would I feel if that happened to me tomorrow, I asked myself.

When I saw the strength and courage of all the patients I met, I thought of the pettiness of most of my worries. And, slowly, I got better at talking to these patients by watching the gentle, caring attitudes of the attending physicians.

I assisted on many more operations. I had the unenviable job of holding a patient's leg while the resident performed a BKA, or below-the-knee amputation. When the leg finally came off, after some gruesome and bloody sawing, I realized what I was holding in my hands. "Where would you like me to put this?" I asked the surgeon. I told myself I was not going to faint.

"Oh, just put it down on the table there."

I dropped the bloody leg on the table, shivering involuntarily as I took my hands away. If I never participated in another amputation, it would be fine with me.

I went along with the other surgeons to see how the patient was doing. "Thanks for staying up all night with me, Doc," he said. I felt foolish and proud at the same time that the man thought of me *as his doctor.*

I had every third night and every third weekend on call. That meant coming in at eight on Saturday and not going home until my workup was finished Monday night. For three days I did not step outside.

The resident and I were the only surgical people on duty in the hospital. Don was off, so he gave me the list of 40 head and neck patients to see. The other resident had 50 more of his own. We split up, each of us working alone unless I needed help. I talked to the patients, checked their wounds, removed stitches, and wrote basic orders for the resident to sign. By evening, we had caught up on the work and admitted a few new patients.

Then we got a call from the overnight unit downstairs. There was a young man with abdominal pain. I went down to see him. After the resident, attending surgeon, and I examined him, we decided there was a good chance he had appendicitis. But we couldn't be sure. Someone needed to watch him all night, so I was assigned the job.

All night, every two hours, I got up and went down to see how he was doing. I felt his belly, looked at his labs, and asked him about the pain. It was getting worse; he was in agony, pleading for painkiller. I explained that we couldn't give him much, because the amount and location of the pain would tell us whether or not the appendix was about to perforate. We still had to wait and see. At six in the morning I came by again, and this time I didn't go back to sleep. There was no point. Rounds would be starting.

At nine we started to operate. His appendix was red and about to burst. After the case, I went along with the other surgeons to see how the patient was doing. He reached over to shake my hand.

"Thanks for staying up all night with me, Doc," he said. I felt foolish and proud at the same time that the man thought of *me* as his doctor.

Near the end of the month I scrubbed in with Don and Dr. Sumner on a major operation on a soft-spoken reverend from Vermont. We removed tumor from his face, did plastic surgery to repair the defects, and checked the neck for tumor metastasis.

I closely watched the face for twitches that would indicate a nerve had been disturbed—and simultaneously held a small retractor, gently pulling the skin back while the two surgeons dissected along the facial nerve. I tried to move and stretch my back muscles as I kept my attention on the patient's face and my grip on the retractor, and I tried stretching up on my toes to help the growing ache in my feet. My face grew damp under the mask, and I couldn't breathe well.

As we finished, Don asked me if I still wanted to be a surgeon. The three of us had stood there working for eight straight hours. My back ached, my feet hurt, my hand and elbow were stiff, and I had pangs of hunger in my stomach—but I didn't hesitate. "Yes," I said. "Even though right now my back is killing me, I still want to be a surgeon."

By that time in the rotation, I didn't have any illusions about surgery. I knew it was going to be tough. I knew that as a woman I would still be a rarity, standing out in conferences, always on display, always being measured up to see if I could take it. I didn't care. I wanted to do surgery. □

HARVARD MEDICAL SCHOOL ANNOUNCES

The William O. Moseley, Jr. Travelling Fellowship

Applications Invited for 1985-86

THE BEQUEST OF JULIA M. MOSELEY MAKES AVAILABLE FELLOWSHIP FUNDS FOR GRADUATES OF THE HARVARD MEDICAL SCHOOL FOR POSTDOCTORAL STUDY IN EUROPE.

In considering candidates for the Moseley Travelling Fellowship, the Committee on Fellowships in the Medical School will give preference to those Harvard Medical School graduates who have —

1. **Already demonstrated their ability to make original contributions to knowledge.**
2. **Planned a program of study which in the Committee's opinion will contribute significantly to their development as teachers and scholars.**
3. **Clearly plan to devote themselves to careers in academic medicine and the medical sciences.**
4. **Individuals who have already attained Faculty rank at Harvard or elsewhere will not ordinarily be eligible for these awards.**

The Committee has voted that within the funds available the amounts awarded for stipend and travelling expenses will be determined by the specific needs of the individual.

There is no specific due date for the receipt of applications or for the beginning date of Awards except that the Committee requests that applications not be submitted more than 12 months in advance of the requested beginning date and in any event not later than December 31 of any calendar year. The Committee will meet once a year in January to review all applications on file. Applicants will be notified of the decision of the Committee by January 31.

Application forms may be obtained from, and completed applications should be returned to:

Committee on Alumni Fellowships in the Medical School
Harvard Medical School
Building A — Room 414
25 Shattuck Street, Boston, Massachusetts 02115

GENETICS

□

THE YOUNGEST BASIC SCIENCE

Taking Stock of a New Department

□

by Lisa Derman

THE LABORATORIES OF Harvard Medical School's new Department of Genetics look no different from ordinary labs. Large rooms contain long, black-topped tables well stocked with beakers, test tubes, and other familiar equipment. Young people in jeans and white coats bend intently over their work or confer quietly in twos and threes. Nothing betrays that the research here is at the leading edge of an explosion of scientific knowledge bearing tremendous implications for medicine, agriculture, and industry.

"What is there, really, that is not touched in one way or another by genetics?" asks Philip Leder '60, chairman of the department and John Emory Andrus Professor of Genetics. The first new basic science department at HMS in almost 20 years, it has expanded rapidly since its inception in December 1980, and has already made several important scientific advances which have applications in such diverse fields as immunology, embryology, and oncology. It also, last year, introduced the medical school's first major course in genetics. Though still in its infancy, the department has attracted two large industry grants, one at the Quadrangle and one at Massachusetts General Hospital, and is participating in the construction of a new building at each location.

Attempts to establish a department of genetics began with Dean George Packer Berry's Center for Human Genetics, headed by Bernard D. Davis '40. In 1977, Davis chaired an inter-faculty Working Group on Genetics, which found that HMS had less extensive teaching of genetics than other medical schools, and stressed the need for a department of genetics. Daniel C. Tosteson made the creation of the new department one of his first missions as dean; just seven months after he arrived at HMS, he convened a group of faculty and outside consultants to discuss

Architect's sketch of the Biosciences Research Building, four floors of which will house the branch of the Department of Genetics in the Harvard Medical Area. The two-story pavilions of the original Brigham and Women's Hospital are now gone; the proposed three-story Ambulatory Services II, at left, is likely to be relocated.

the matter. Upon his recommendation, the faculty voted in October 1978 to establish the department.

In the meantime, genetics research continued to grow at HMS. Today, in addition to the work in the Genetics Department, molecular genetics research is concentrated in the departments of Biological Chemistry and Microbiology and Molecular Genetics, and in cancer research labs, though some is going on in virtually every department and teaching hospital. In Cambridge, much of the genetics work is done in the Department of Biochemistry and Molecular Biology, which dedicated its new building three years ago.

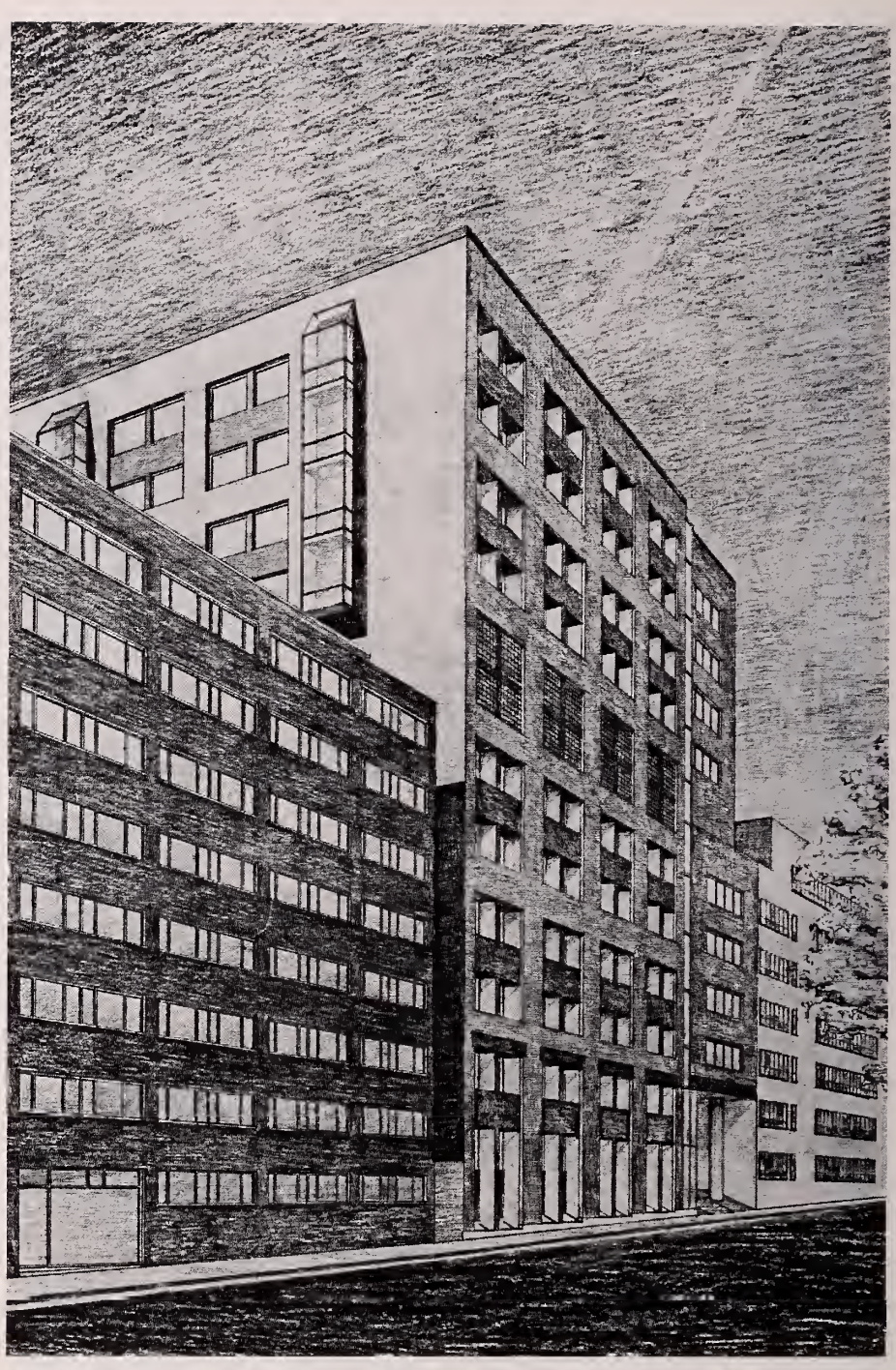
In 1980, a search committee appointed by Dean Tosteson and headed by Nobel laureate Baruj Benacerraf found in Philip Leder a candidate "ideally suited to undertake the leadership of the Department of Genetics." Leder's scientific career had begun in 1956 with his Harvard College honors thesis on the interaction of steroids with nucleic acids, the fundamental chemicals of DNA. It was still "the dawn of the era of molecular genetics," as he phrases it, shortly after Watson and Crick's discovery of the double-helix structure of DNA.

Although Leder spent his summers at the National Institutes of Health (NIH) and squeezed in as much research as possible during his years as a medical student, intern, and resident, he had not yet settled on a future direction. He reached what he calls "the dramatic turning point" of becoming irrevocably committed to genetics research in 1962, as a fellow at NIH.

"I fell in with a young fellow who was trying to show that there is such a thing as messenger RNA," Leder recalls. "His work was tremendously interesting. I forgot all about working with the other important people at NIH." As it turned out, the "young fellow" was Marshall Nirenberg, and his topic was deciphering the genetic code, for which he was later awarded the Nobel Prize. Breaking the genetic code, Leder remembers, "combined all the drama of a thriller movie with all the excitement of a scientific discovery. I was hooked. I couldn't stop."

Leder remained at NIH for 18 years, eventually becoming chief of the Laboratory of Molecular Genetics at the National Institute of Child Health and Development. NIH honored him with its Director's Award in 1976 and its G. Burroughs Lectureship Award in 1977, the year he and colleagues reported the first successful cloning of a mammalian gene. His many other honors include the Warren Triennial Prize of the Massachusetts General

"What is there, really, that is not touched in one way or another by genetics?" asks Philip Leder '60, chairman of the new department.



Artist's rendition of the Wellman Research Building. The Department of Molecular Biology's permanent laboratories will be in the upper four floors.

PHOTOS COURTESY MASSACHUSETTS GENERAL HOSPITAL

Hospital in 1980 and the National Academy of Sciences' Richard Lounsbery Award for Biology and Medicine in 1981.

The Genetics Department has grown quickly since Leder's appointment as chairman in December 1980. It now includes three tenured and four junior faculty members, 36 postdoctoral research fellows, and 22 graduate students. These students, like all HMS graduate students, receive their degrees through the Faculty of Arts and Sciences, but do their work in a medical school department.

The branch of the department at the Quadrangle is temporarily housed in the Laboratory for Human Reproduction and Reproductive Biology next door to Building A. Ground has already been broken directly across Shattuck Street for the new Biosciences Research Building, a 15-story complex that will hold the permanent labs. The new building, a joint venture of Brigham and Women's Hospital, Howard Hughes Medical Institute, and HMS, is scheduled for completion in August 1985.

The MGH branch of the Genetics Department, the hospital's Department of Molecular Biology, chaired by Howard M. Goodman, will have new quarters in the upper four floors of the 11-story Wellman Research Building, also under construction. The lower floors will house other research departments of the MGH.

PROGRESS IN GENETICS HAS BEEN extremely rapid; keeping abreast of developments is difficult. "I did laboratory research when I was in college," says Patricia Thistlethwaite, an M.D.-Ph.D. student in Leder's lab. "But when I returned to laboratory work after two years of medical school, things had changed so much that I essentially knew nothing." Leder's lab holds weekly seminars, at which a member of the department or a scientist from another institution presents his or her latest work.

Leder and his colleagues have discovered precisely how the shuffling of a few hundred genes directs the building of literally millions of different antibodies: the antibody molecule is constructed in several parts, each of which can be shuffled in any one of several genetic arrangements. The various combinations of alternative parts allow for what Leder has called the immune system's "virtually unlimited capacity to generate different antibodies."

Since malignancy in antibody-pro-

The Wellman Research Building under construction.

Greenhouse of the Department of Molecular Biology's temporary labs, in the Jackson Building.

ducing cells is involved in many leukemias and lymphomas, the investigators are now directing their attention to these diseases. They have developed very refined tests that place leukemias and lymphomas in various diagnostic categories according to the arrangement of their immunoglobulin (antibody molecule) genes.

One of the diseases they work with, Burkitt's lymphoma, involves a genetic translocation: the endpieces of two chromosomes break off and exchange places. While studying the genetics of immunoglobulin in Burkitt's lymphoma, research fellow Rebecca Taub and colleagues in Leder's lab experienced what the *Boston Globe* called "a bit of scientific serendipity": they found a clue to what causes the malignancy. The exchange of genetic material, they discovered, moves an oncogene—a gene associated with cancer—from one chromosome to the antibody-producing location of another.

Breaking the genetic code, Leder remembers, "combined all the drama of a thriller movie with all the excitement of a scientific discovery. I was hooked."

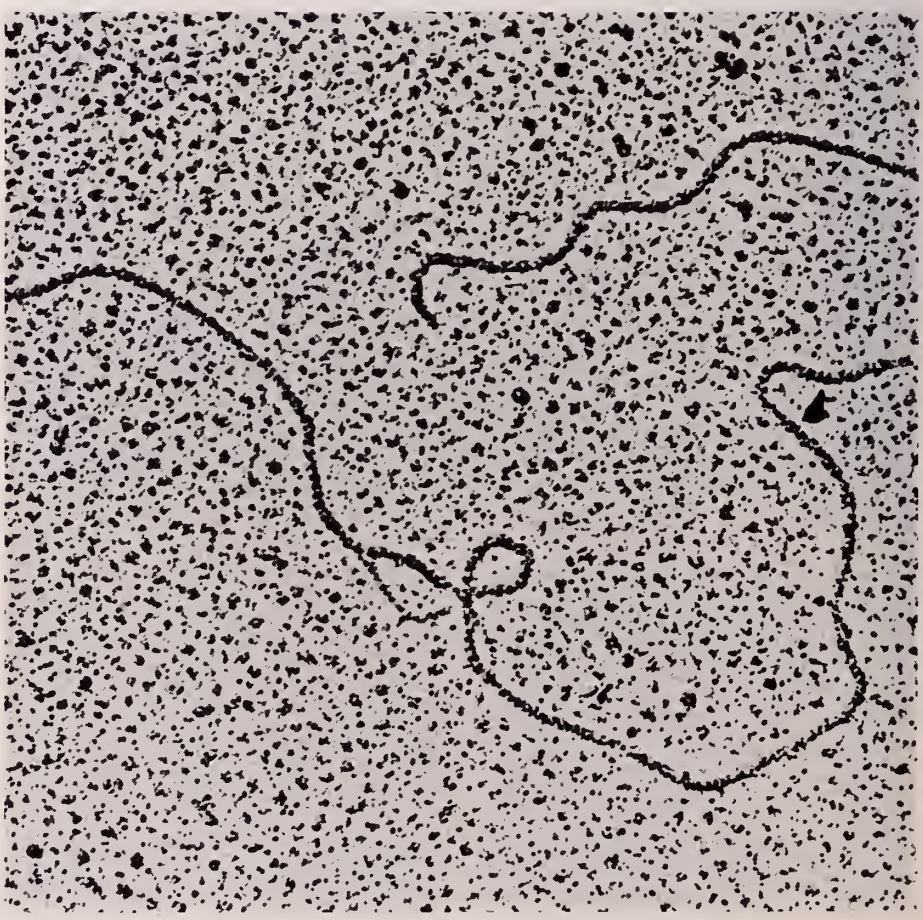
"It's as if you plucked someone from the side of a peaceful, calm New Hampshire lake and dropped him into the middle of Times Square," describes Leder. He speculates that the intense activity of the antibody-producing site somehow turns on the oncogene, called the *myc* gene.

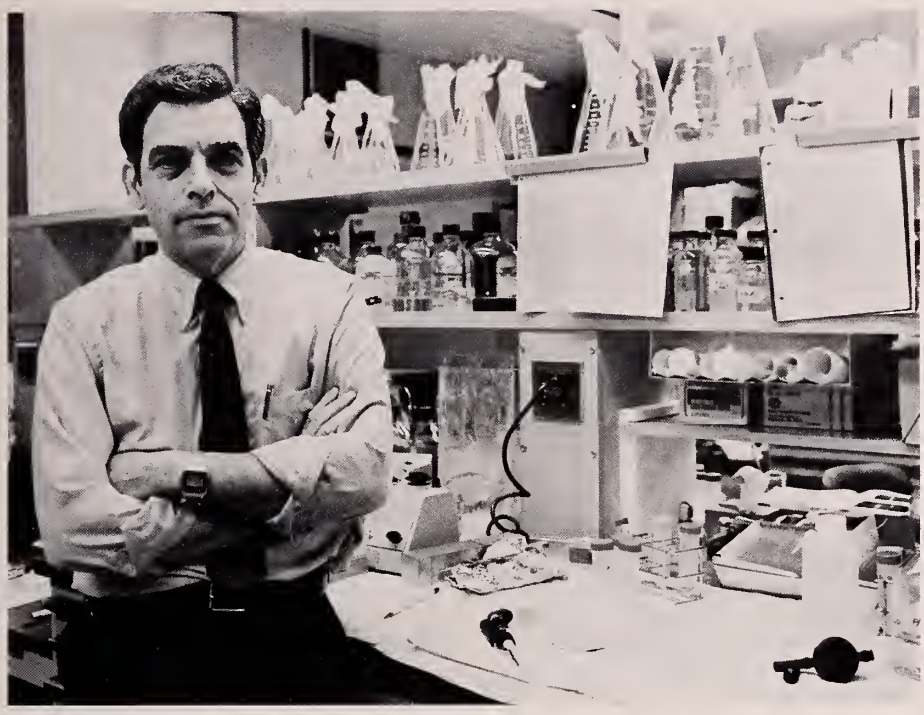
Just a few months ago, investigators at the Dana-Farber Cancer Center found another oncogene that is activated in Burkitt's lymphoma. They hypothesize that the malignancy is a two-step process: activation of one oncogene sets the stage for the cancer, but it is not until a second oncogene is activated that cancerous growth actually begins. This theory, which is similar to a two-step theory of cancer development put forth by investigators at MIT and the Institute of Cancer Research in England, could explain why cancer often takes years to develop.

I'M VERY FORTUNATE TO HAVE A lot of very effective and intelligent people working with me," Philip Leder comments. "It's an open secret that HMS is what it is because of its undergraduate medical students, graduate students, and fellows in training. They are one of the great strengths of this institution, maybe the most important one. Often all you have to do is get out of their way."

Twelve post-doctoral fellows, two graduate students, and two M.D.-Ph.D. students in the Health Sciences and Technology (HST) program carry out the actual benchwork in Leder's lab. Leder oversees all the work, overcoming technical hurdles, inter-

Above: computer-generated model of antibody molecule, courtesy of Richard J. Feldmann of NIH. Below: mouse genes for alpha-globin and beta-globin (components of hemoglobin) bound together in a double strand; the "bubbles" form where the two genes differ. (Electron micrograph courtesy of Philip Leder).





Philip Leder

PHOTO BY LORIE NOVAK

preting results, offering suggestions for the next step in the research.

All of the research now under way in the lab involves immunoglobulin or the *myc* oncogene (the gene that apparently is instrumental in Burkitt's lymphoma). For example, post-doctoral fellow Tim Stewart injects the *myc* gene into mouse oocytes (egg cells) under a high-resolution microscope, to see if the mice that are born develop cancer.

M.D.-Ph.D. student Patty Thistlethwaite is also working with the *myc* gene. Scientists have long suspected—and, in a few specific cases, have demonstrated—that oncogenes, which exist in every cell in the body, turn on during normal embryonic development, and then turn off. "The embryo is similar to cancer in that it 'invades' an area and then rapidly proliferates," Thistlethwaite explains. She is trying to determine at what stage, and in which organs, the *myc* gene is expressed normally in mouse embryogenesis.

In order to accomplish their research goals, the students and post-docs in Leder's lab spend their days—and often their nights as well—doing painstaking procedures that reveal information about the gene of interest and are also preliminary to other techniques, such as cloning. They mix tiny quantities—microliters—of DNA (usually mouse DNA) with a restriction enzyme, which cleaves it at specific sites into various sized pieces. They then separate the pieces by size through electrophoresis: an electric current carries the DNA through a gel, moving the smallest pieces the farthest. To locate the size piece of DNA that contains the gene of interest, they introduce a radioactive "probe"—a piece of DNA or RNA that will bind to the desired region—and allow the radioactivity to expose photographic film.

Once investigators have determined what size piece of mouse DNA contains the desired gene, they repeat the whole process with a larger quantity of DNA, and extract the proper size pieces. Then, using techniques developed just five years ago, they can clone the gene. In the cloning process, they first cleave the pieces of DNA and a bacterial virus (called bacteriophage, or simply phage) with the same restriction enzyme, so two ends of the phage bind to each piece of mouse DNA, creating a virus that contains mouse DNA. After the virus has grown in a culture, investigators use a radioactive probe to reveal the location of the desired gene, and simply remove it in an ultra-fine pipette. If they want more of it, they can introduce it to a fresh culture and continue to let it grow.

To learn the structure of their cloned gene, investigators can use chemical techniques to sequence it: that is, to determine the precise order in which thousands of molecules of four chemical bases (adenine, guanine, thymine, and cytosine) line up to form that particular gene. In his lab, Leder has a yard-long computer print-out listing the 8,200 bases of the *myc* gene, just one of the approximately one million genes in a mammal's DNA.

"When I returned to genetics lab work after two years of medical school," says student Patricia Thistlethwaite, "things had changed so much that I essentially knew nothing."

PREYING ON PUBLIC FEARS OF recombinant DNA technology, a radio advertisement broadcast this past September described a scenario of dangerous genetically altered organisms escaping from a Harvard lab and infesting Cambridge. The event is fictional: it is a scene from a new thriller novel, *Spirals*. But another part of the book, dealing with controversy over the research, is based on a true incident. In 1976, Cambridge mayor Alfred E. Vellucci's complaints about potential danger from escaping organisms led to a temporary moratorium on such research and the installation of new safeguards at Harvard labs.

The controversy over recombinant DNA research is no longer as heated nor as widespread as in 1976, but it continues nonetheless. For example, columnist Liebe F. Cavalieri expresses concerns about safety in striking terms. "From their laboratories, microorganisms with properties taken from higher forms of life will inevitably escape into the ecosphere," he writes in one column, printed in the *Washington Post*. "We are laying the groundwork for unforeseen evolutionary changes that may create an

inhospitable environment for present species."

Investigators generally dismiss such alarmism as uninformed. Phil Leder points to the NIH guidelines on genetics research, which require the use of specially weakened bacteria that cannot survive outside the laboratory. The guidelines define four levels of danger, and specify precautions to be taken at each. Almost all HMS genetics research is at the first two, low-containment levels.

One example of research at the highest containment level is that of John R. Murphy, associate professor of microbiology and molecular genetics at HMS (not part of the Genetics Department), who received NIH approval to insert the diphtheria toxin gene in a strain of *E. coli* genetically altered so that it cannot live outside the laboratory. His research will take place in a special high-containment laboratory in Ft. Detrick, Maryland. Harvard has no facilities for research at the fourth containment level because of the prohibitive cost.

"I know of no example of any laboratory infection or deleterious effect that has occurred as a consequence of using recombinant DNA technology, and indeed I would not expect to find any," Phil Leder replies to a query about potential hazards. "Recombinant DNA technology usually does not in itself make something more dangerous than it already is; in fact, very often it makes it far less dangerous.

In return for its HMS grant, Du Pont gets "a window on science" and exclusive license to market any inventions arising from the research.

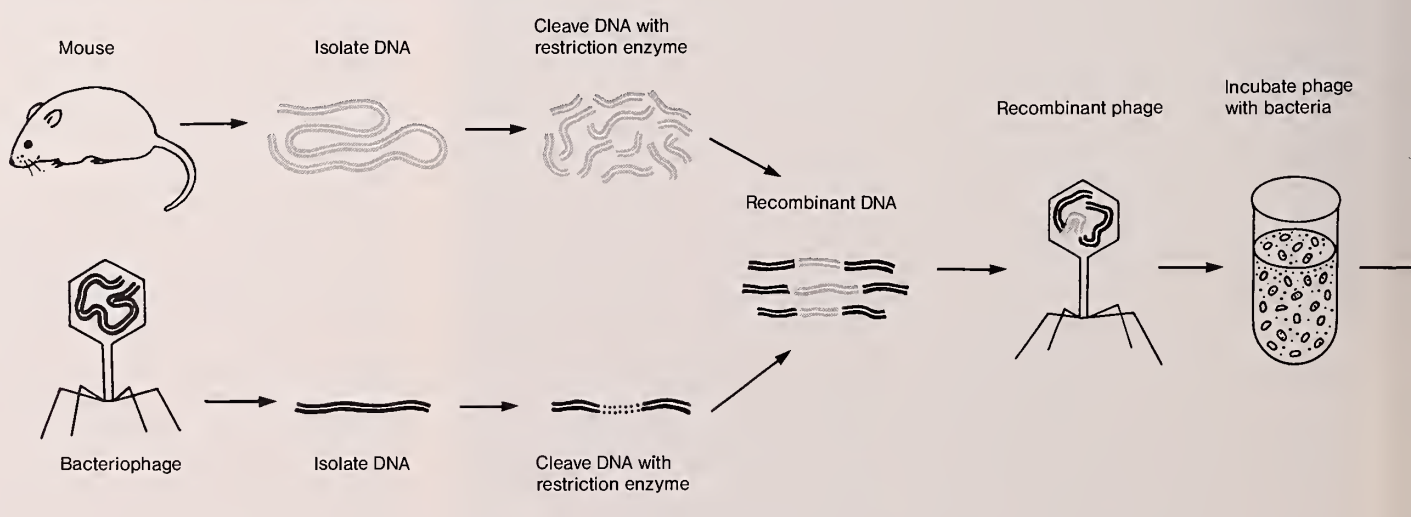
"If you study the hepatitis virus using recombinant DNA technology, you can remove only the part you wish to study. Since you have deleted all the other genes that are necessary for its expression, the virus becomes entirely benign, non-infectious. Still, if you're dealing with any pathogen—and most genes are *not* dangerous—you have to apply those elements of containment that are applied to it in its normal genetic environment."

Though the guidelines apply only to research done with NIH funds, other researchers (mostly biotechnology companies) generally voluntarily adhere to them. Unwilling to rely on voluntary compliance, and lacking national or statewide regulations of recombinant DNA research, several Massachusetts cities (including Boston, Cambridge, and Newton) have passed their own ordinances, the main effect of which has been to lengthen the review procedure.

POTENTIAL HAZARDS ARE JUST one controversy surrounding genetics research; another concerns private industry's involvement. This involvement takes two forms, neither of which is either new or unique to genetics. Faculty in many fields have long worked as consultants, and industry has supported research at universities for decades: in 1974, for example, the Monsanto Company pledged to give HMS $23 million over 12 years for research on the biology and biochemistry of organ development.

Yet nowhere has the injection of corporate money been more dramatic than in the field of genetics. Industry was almost totally disinterested in molecular biology until about 1977, the *Economist* reports. Then geneticists started making huge strides toward genetic engineering feats that were the stuff of science fiction only a decade ago: inserting the insulin gene into diabetics, for example, or creating a new strain of disease-resistant plants. Suddenly recognizing the potential for enormous profits, business began to pour hundreds of millions of dollars into university-

How to Clone a Mouse Antibody Gene



based genetic research. "We don't see that corporate funding can replace federal support on a dollar-for-dollar basis," explained Alan C. Olsson, HMS dean for resources, when announcing a large industry grant for the Genetics Department, "but it is complementary."

This sudden influx of money has brought long-ignored ethical questions to the fore. How much time should a professor spend on outside consulting? Is there a conflict of interest when a faculty member owns a significant part of the company that is funding his or her research? To what extent should a funding company dictate the terms of research done under its grant?

The Hoechst grant, which exclusively funds the MGH's Department of Molecular Biology, was first solicited by Howard Goodman when he was still on the faculty at UCSF.

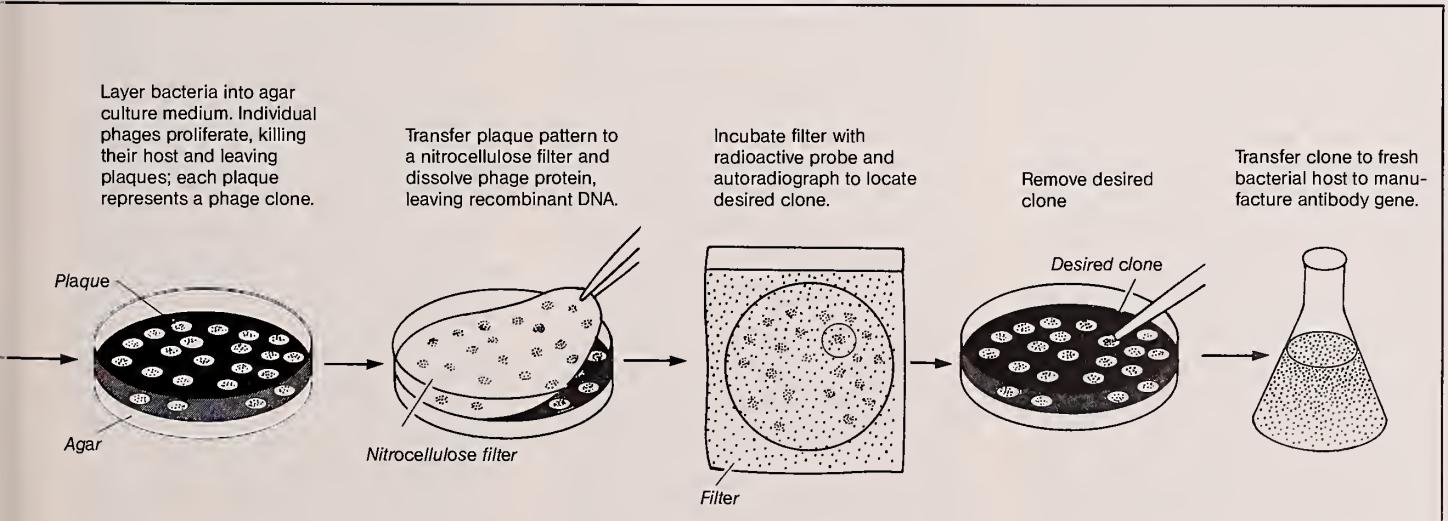
In the spring of 1982, Harvard University president Derek Bok met with the presidents of Stanford, California Institute of Technology, MIT, and the University of California to discuss these and other issues. Harvard then established its own Guidelines on Research Conducted with Industry, specifying conditions for conducting research, maintaining academic freedom, avoiding conflicts of interest, ensuring quality, and regulating patent licensing.

Along with grants from a number of sources, including NIH and a new private foundation called the American Business Cancer Research Foundation, Phil Leder's lab is supported by a five-year, $6 million grant from Du Pont. "There are no provisions in the grant that will in any way control, inhibit, or restrict the conduct of the research or publication of the results," Du Pont officials assured when they announced the grant in June 1981. Indeed, the terms of the contract specifically protect these academic freedoms. Faculty members direct the course of their own research, and are free to communicate results and techniques and to publish papers. Du Pont may not impinge upon the selection or appointment of faculty, which is solely the prerogative of Harvard's Faculty of Medicine.

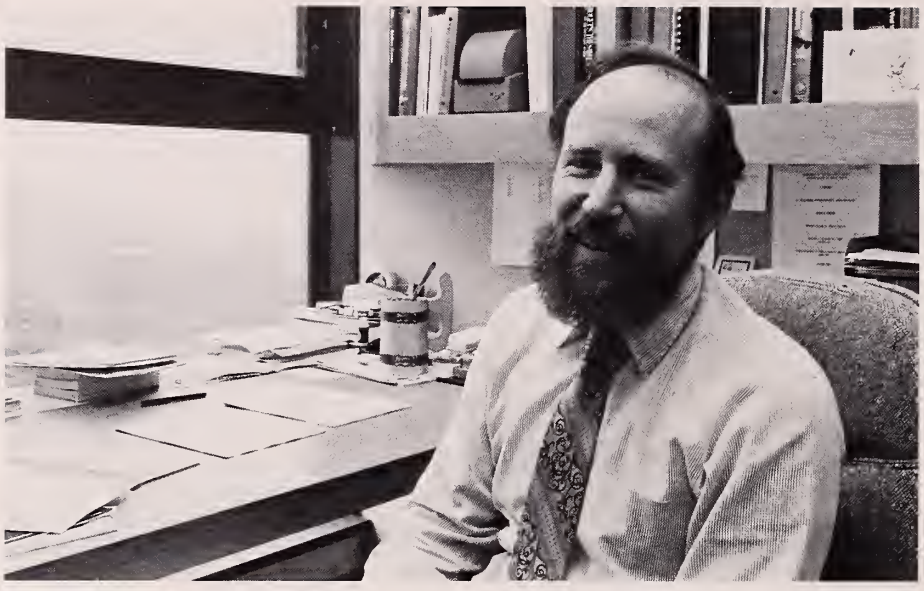
In return for its money, Du Pont gets two main advantages. The first, and most important, is "a window on science": the company can learn about and keep up with the latest discoveries and techniques. Second, should a patentable product or process arise from the research, Harvard would own the patent and Du Pont would have exclusive license to develop and market the invention.

It might appear unfair that a private corporation should reap the profit of an invention made partially at taxpayers' expense. But that is exactly what the government mandates, so that the public will have the benefit of the new invention. As Joyce Brinton, assistant to the dean for finance and business, explains, "It does no good to create a new vaccine for cholera if it isn't marketed—if it doesn't reach people." Federal regulations dictate that the university own any patent arising from federally funded research done by its faculty, and must pursue commercial development. The only practical way for a university to fulfill this obligation is to license marketing rights to a private company.

In accordance with these regulations, Harvard owns all patents on its faculty's inventions. The HMS Technology Transfer Committee, which consists of John F. Taplin, director of technology development; Carl W. Walter '32, chairman of the Alumni Fund; and Joyce Brinton, works in conjunction with the university's Office on Patents and Copyrights to arrange licensing for HMS faculty inventions.



From "The Genetics of Antibody Diversity" by Philip Leder. Copyright © 1982 by Scientific American, Inc.



Howard Goodman

THE GENETICS DEPARTMENT'S most recent industry grant supports the MGH's Department of Molecular Biology. Though part of the hospital, and of the Genetics Department (faculty members of the MGH department are also members of the faculty at the Genetics Department, and fulfill all HMS faculty functions), it is funded exclusively by a 10-year, nearly $70 million grant from Hoechst A.G., an international chemical company based in Frankfurt, Germany.

The unusual history of the Hoechst grant—treated in depth in a recent *New York Times Magazine* article—began at a conference at Ising am Chiemsee, Germany, in October 1980, when geneticist Howard M. Goodman first approached the company with a proposal that it fund a department of molecular biology. Though Goodman's proposal mentioned several sites in the United States, it was most likely that the department would be established at the University of California at San Francisco, where he was on the faculty. Hoechst was enthusiastic.

Coincidentally, the MGH was recruiting Goodman to head its own section of the HMS Genetics Department. Goodman decided to make the move, and told hospital officials about the pending deal with Hoechst. The MGH, while surprised, quickly took advantage of this opportunity to support its research activities, and decided to found its Department of Molecular Biology.

Hoechst was familiar with Goodman and his scientific track record. Goodman had contributed to studies on restriction endonucleases, the enzymes that cleave DNA (and which are essential in recombinant DNA technology), and had been a member of the team at UCSF and Stanford that first described recombinant DNA technology. He and colleagues were the first to clone both the human growth hormone gene and the human gene for insulin. In the late 1970s, he had done some consulting work for Hoechst in relation to insulin cloning.

The Hoechst agreement protects the basic academic freedoms in much the same way as the Du Pont agreement. Direction of research, communication with other scientists, and appointment of faculty members are all completely outside of Hoechst's control. Hoechst does require that it see drafts of manuscripts 30 days prior to submission for publication, but has no say in whether papers may be published.

Like Du Pont, in return for its money Hoechst gets an opportunity to learn about the latest developments. Should any patentable inventions arise in the course of the research done inside the department, the hospital will own the patent and Hoechst will be granted exclusive worldwide license to market it. Unlike Du Pont, Hoechst also has the right to send up to four of its scientists at any one time to be trained in the Department of Molecular Biology.

Are U.S. taxpayers partly footing the bill for research that may eventually profit a foreign corporation? To answer this question, Congressman Albert Gore, Jr. (Democrat of Tennessee), chairman of the subcommittee on investigation and oversight of the House Committee on Science and Technology, asked the U.S. comptroller general to examine the Hoechst-MGH contract. The comptroller found no legal conflict as long as no federal money supports the department—which is just what the Hoechst exclusive funding of the department provides.

Howard Goodman believes that Hoechst will continue to fund the department after the initial 10-year grant, though continuation is by no means certain. "None of us can second-guess what's going to happen to any business seven or eight years from now," he points out, listing the advantages the Department of Molecular Biology will have gained even without renewal of the funding: 10 years of supported research, all the laboratory equipment, and a permanent laboratory in the new Wellman Research Building.

Although Hoechst may not direct research in the lab, won't Goodman and colleagues be tempted to do the kind of work most useful to the company, in order to ensure renewal of the grant? Goodman thinks not. "If anything, the pressures are the opposite," he says, "such as going overboard to do more esoteric things, to do some science that might be a little chancier," because the grant covers such a long period.

Current research in Goodman's lab covers a wide spectrum of plant and animal genetics. He and colleagues participated in experiments on the genetic exchange by which a bacterium causes crown gall tumors to form in plants. Now he is asking an even more basic question: "What makes a leaf a leaf, a stem a stem, and a root a root?" He is also working with genes that control plant enzymes, such as one that makes variant plants resistant to a certain herbicide. He hopes eventually to be able to transfer this trait to other plants.

Frederick M. Ausubel, professor of genetics, is studying bacteria that interact with legumes, enabling them to take nitrogen from the air, where it is plentiful, rather than compete with other plants for the relatively scarce amounts in the soil.

PHOTO BY LORIE NOVAK

On the animal genetics side of the lab, investigators are working with genes for receptor proteins. These proteins allow a cell to recognize certain compounds, such as insulin, in order to bind them and move them into the cell.

EVEN WITH THE RAPID PACE OF progress in molecular genetics, gene therapy—curing disorders such as thalassemia or diabetes by replacing a defective gene—is still a long way off. As reported in a recent issue of *Nature,* it is now possible to introduce a new gene (for example, the gene for rat growth hormone) into a single-cell mouse embryo and observe the effects (larger mice). Investigators can also introduce DNA into a cell and then reintroduce that cell into an organism. But they lack the crucial ability to control how and where in the body the new gene will be expressed.

As the potential for gene therapy is realized, it will raise ethical questions: how should it be used, and who should benefit? What about the still very remote possibility of eugenic uses—"designing" human beings, controlling behavioral traits? HMS's Bernard Davis has been one of the leading scientific spokesmen on these issues for many years. Back in 1970, he weighed the potential for abuses of genetic engineering, since "we can hardly assume that a high level of civilization provides a guarantee against such an evil use of science." He found that, for many scientific as well as moral reasons, such dangers are extremely unlikely.

Moreover, unlike atomic physics—to which alarmists often compare it—genetics is not developing in secret, outside the realm of social control. The traditional academic freedoms—and the new industry/academe arrangements at HMS—assure that information about new discoveries will reach the public, so that the public can decide how best to apply new technologies. As Davis declared, "if and when gene transfer in man becomes a reality, there would still be time to assert the cultural and medical traditions that would promote its beneficial use and oppose its abuse."

Today, Congress is considering creating a permanent commission to monitor human genetic engineering. In a recent *New York Times* Op-Ed

As the potential for gene therapy is realized, it will raise ethical questions: How should it be used, and who should benefit?

piece, Davis argued: "A commission with such a narrow assignment might have to invent things to do. Its existence would likely arouse false fears, for there are always people eager to stir up anxiety, and genetics is a favorite target." He pointed out that practical considerations suffice to limit human germline intervention. Instead of a commission he urged continued philosophical discussion, so that we, and future generations, can respond appropriately to ongoing developments.

In the meantime, progress continues in genetics research, with the HMS Genetics Department in the forefront. And the department still has a lot of growing to do.

"We will probably in the future have genetics appointments at other hospitals," Leder projects. "I'm looking forward to such appointments at Children's Hospital, for example, and I hope eventually at Brigham and Women's Hospital. We're very broad in our definition of 'geneticist,' and that allows us to incorporate those who take care of children with inherited diseases, who do pre-natal counseling, and who work on molecular aspects of genetics in cells in culture or in microorganisms."

The HMS teaching hospitals provide many clinical genetic services. Children's Hospital and the MGH both have comprehensive clinical genetics facilities, where, for example, counseling is offered to people with a family history of a disease, or to pregnant women who have been exposed to a drug or radiation. Patients with known or suspected genetic disorders are referred for surgical treatment or to social agencies when appropriate. Not many of the more than 3,000 known genetic disorders are yet treatable, but some can be treated in utero.

Recombinant DNA technology has entered the clinical sphere in the diagnosis of sickle-cell anemia and thalassemia. DNA isolated from amniotic fluid drawn from the uterus is studied in vitro to determine whether mutation has altered the order of the genes, as is characteristic of these diseases. Similar techniques hold promise in the diagnosis of other diseases, such as Huntington's chorea, in the near future.

"Ten years ago, molecular genetics had only distant relevance to the diseases of man," summarizes Phil Leder. "Today, hardly a month goes by in which molecular genetics doesn't appear in the *New England Journal of Medicine.* Genetics has become an important tool for understanding, for diagnosis, and even for treatment. It's something every physician should know about." □

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Two Stories

by Max Eddy

Last year, after the death of his good friend Maxon Eddy '35, George (Barney) Crile, Jr. '33, organized a private collection of Eddy's writing. Modestly titled Selected Works of Max Eddy, *dedicated to "Virginia, who shared Max's travels, and made it all possible," the collection is prefaced with an introduction by Crile which reads in part:*

"For three years Max Eddy was the right tackle on the Yale football team. Intermittently I played next to him at right end. Then we went to Harvard Medical School together, and from there on to Cleveland for further training in surgery. Our wives had been classmates at Smith College.

"With fascination and admiration I followed Max's medical career. He was the leader of his community in surgery. Then, at the time he was gaining national acclaim, he decided to travel. It was not only with a missionary's zeal that he took his talents to so many of the underdeveloped areas of the world, but also with an overpowering sense of humanity and of curiosity to see what he could learn from others.

"As his writings so clearly portray, Max had a talent for understanding people and a genius for recording his thoughts and the deep emotions that motivated him. This collection represents only a fraction of his writings. In this selection is condensed the spirit that drove Max to and through a superbly successful medical career. It is my hope that his friends will enjoy this recapitulation of the life of a great man."

In the first of the two pieces reprinted here, an excerpt from a longer story, Eddy recounts his first close experience with illness and death—an experience closely linked to his childhood impressions of his father's medical practice. "My father was a general practitioner whose office was in the home," he explains in another story. "During busy office hours his medical activities often spread out through the house. Babies were delivered in the parlor and dislocated joints were reduced in the front hall. I remember an Italian sculptor, Angelo Gatti, from the marble works sitting at the dining room table singing arias from La Traviata *while soaking his injured hand in a stew pan full of antiseptic solution."*

The second selection, "Guts," draws on Eddy's years in developing countries. Of his decision to take his skills abroad, he wrote, "Buried dreams came alive again in the promise of high adventure and new accomplishments." When he first arrived in Gondar, Ethiopia, he was the only surgeon at the only hospital for three and a half million inhabitants of the province of Begemedir.

"Our first reaction to the bewildering culture," he writes, "was a numbing shock. After less than 24 hours' traveling time, the pace abruptly slowed from 500 miles an hour in the air to the weary gait of an old woman carrying on her back a 75-pound cask of water. On her face and in her staring eyes was imprinted the pain of thousands of her sisters who, like her, had suffered during most of their lives from the raw bleeding grooves across their chests and shoulders gouged by thongs lashing the burdens to their backs. Poverty and ignorance were appalling: beggars were everywhere. Belief in witch doctors (wageshas) was deep-seated and almost universal."

As he got to know the people, he became familiar "with their simplicity and directness, their traditional courage and pride, their humor, and above all, their faith in the natural process." "Guts" draws on that familiarity to evoke an Ethiopian's experience with, and attitude toward, the medicine of the "white foreign doctors."

ILLUSTRATION © E. SLOTE 1983

To Angelina, with Love

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One evening Pop's office bell rang. I was the only one in the house, for some reason, and answered the bell. When I opened the door, standing there was a woman holding the hand of a girl about my size.

"We come to see Mista Dott. We have an appointment," the woman said.

I showed them into the reception room and told them my father would see them soon. The mother sat down in a large chair and the girl stood beside her. I pulled a smaller chair over beside the mother.

"You can sit here," I said to the girl.

She wriggled up onto the chair and flattened her green skirt down over her knees.

I pulled another chair over beside her.

"Can I sit here?" I asked.

The girl looked at her mother, who smiled at me and nodded. I sat in the chair.

I kept leaning forward and looking at the girl beside me. She had large, dark-brown eyes. Her cheek bones were prominent and flushed—peach colored. She had full strawberry colored lips, and I could see that all of her front teeth were in and white. When I noticed how small her ears were, I became conscious of the size of my own, and pushed them back against my head. Her black hair hung down her back to her waist in two ponytails tied with multi-colored ribbons.

"What's the trouble you got?" I asked.

Her mother answered, "She's got a fever."

"What grade you in?" I asked.

"Fifth."

"I'm in the sixth," I said, looking at the floor.

"You are not. You're in grade four room."

A long interval of contrite silence on my part followed such a devastating and ignoble defeat. But at eight, the past is a fleeting moment, the spirit is resilient and the future is always bright.

"Your father work at the marble mill?"

"Uh-huh."

Her mother said, "He carves mar-

After the school year ended, I asked Pop almost daily when Angelina was coming to the office. Whenever she did, I managed to get into the reception room and sit with her for awhile.

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ble. He's a sculpt. We from Italy—two years. He's a very good sculpt."

The Middlebury mill of the Vermont Marble Company was the largest enterprise in our town. It turned out cemetery monuments. The artists and craftsmen who came directly from Italy carved beautiful designs and statues. Pop had taken me through the mill a number of times. And sometimes I had gone there by myself.

Watching the creation of those miracles from marble blocks was like seeing a figure slowly emerging from a dense white fog, barely discernible at first, then gradually becoming distinct and clearly outlined. There were many forms of the crucifixion, birds, intertwining vines and leaves, and the Madonna, sitting or standing. And there were angels—angels everywhere.

"Who's your father?"

"Montanelli. Angelo Montanelli," her mother answered.

"What's your name?" I asked the girl.

"Angelina. Angelina Montanelli," she replied.

I wanted to ask her if I could watch her father at his work some day, but Pop opened the door into his office then, and I knew I had better leave.

After the school year ended in June, I asked Pop almost daily when Angelina was coming to the office. Whenever she did, I managed to get into the reception room and sit with her for awhile. Her mother came with her; sometimes we just sat there saying nothing to each other.

One time Angelina was by herself. When she came out of the office, I was waiting for her.

"Want to see my new lamb?" I asked.

"Sure. Where is it?"

I led the way a few hundred feet through the back yard down to the barn. When I began to run, she said, "You go ahead. I gotta walk."

I came back to walk with her.

"Why?" I asked.

"My fever. I get tired."

We went to the sheep shed where I brought the one-week-old lamb to her. We sat on an old foundation beam of the shed while she held the lamb in her lap.

When she leaned over and rubbed its nose with hers, I said, "Lucky lamb."

"What do you mean?" She squinted her eyes and laughed.

"What's his name?" she asked.

"It's a ewe," I said.

"What do you mean? It's a me?"

"No. I mean it's a girl."

"O-oh. I'm going to name her Angelina. Do you like that?"

"Gee," I said, "that's a good name. Angelina Lamb."

We both reached out to pat the lamb. My hand touched hers. We looked at each other and my face turned red. I jumped up and ran out to the back yard. She followed soon, slowly. It was uphill, and when she joined me in Mom's flower garden, she was breathing hard.

"You like roses?" I asked.

"My mother misses her flowers in Italy," she replied.

"I'll pick some for her."

"No. Don't. Don't pick flowers. Let them grow. Let everything live as long as they can."

There was a strange expression on her face. I didn't understand. Much later, when I remembered what she had said about the flowers, I wondered if she knew then what was happening to her.

"I'll take my mother some 'sparagus tops. It's old and no harm to cut."

In our back yard Pop had put up five birdhouses for purple martins, beautiful birds in the swallow family. From their arrival April 20th, to August 20th when they went south, their cheery, melodious songs filled the air of the back yard, and we watched their graceful flights as they soared through the air.

I told Angelina how much I liked to watch the martins. We went over under the birdhouses and sat on the grass.

"Each martin eats 2,000 mosquitoes a day," I told her.

"Where do they get them?'

"You lie on your back and look way up in the sky." Both of us lay back on the warm, soft grass, looking up into the cloudless blue sky. "See the birds up there? Little specks—way up there—catching bugs and mosquitoes?"

Finally she could see them. As we watched, one by one the birds plummeted from the sky with wings almost folded—"like stones," Angelina said—until just before landing at their entrance in the birdhouse, when they spread their wings in time to check their fall.

"Their mouths are full of bugs," Angelina said.

"Those are to feed the young ones in the nest."

We stood up. "They're pretty," she said. "Can I come and watch them again?"

"Come tomorrow. I'll wait for you."

We walked up the driveway from the barn to the street. She left and walked down the street in front of the house. I yelled after her, "Any time," but she didn't hear me.

After a month or so, Angelina didn't come to the office anymore. Pop said she had to stay in the house. The next time he visited her, he took me with him.

When we drove up in front of a strange house, I asked, "What are we doing here?"

"Angelina is staying here now," Pop said. "It is better for her. She is with people who can take care of her. She is not strong and spends most of the time in bed."

What's the matter with her, Pop?" I asked.

"She has trouble with her blood. She can't make good blood, and it leaves her weak," Pop explained. "It's called Mediterranean anemia."

"Gee, I can't even pronounce that. Can I see her?" I asked.

"Of course you can. You come with me."

We went into the house. Angelina was sitting up in bed. Pop went over, patted her head, and then, with his arm around my shoulder, said, "Look what I've brought you."

I stood there like a lump. He asked her a few questions and took some blood from her arm with a needle and syringe. I had never seen this before, and when the syringe filled with blood, I slumped into a chair. Angelina didn't make a sound. Next, Pop listened to her chest with his stethoscope. He smiled at her, patted her head again and said, "I guess you'll keep for awhile."

He turned to me. "I'm going to see some other patients here. You stay with Angelina while I'm gone."

I pulled a chair up beside her bed and sat down. Angelina had a shiny look. Her skin almost glistened, and it seemed tight over her forehead, cheek bones, and jaws. Her eyes were bigger and stuck out more. Although her lips were red, they seemed thinner. And her ears looked bigger.

"How are you, Angelina?"

"I'm fine. Just tired," she said.

"Do you sing?"

"Sometimes. Why?"

"I brought my mandolin. I just got it a few months ago. Mom gave it to me. Do you want me to play it and sing?"

"I like concertinas and accordions," she said.

"It's out in the car. Can I go get it?"

"If you want to. Sure."

I went out to the car. Pop was sitting behind the steering wheel reading a journal. When I reached into the back seat to get the mandolin, Pop said, without taking his eyes off his journal, "Take your time, son. I've got a few more patients to see."

I thought that was funny—his seeing patients sitting in the car.

Back in Angelina's room I said to her, "I can't play very well."

"I don't care. It's a pretty thing, isn't it?"

"I can't sing very well, either."

"I don't care," she said.

"Mom made up a tune to some words. You want to hear them?"

"Sure. Play it. I'll bet you don't dare."

I picked a few notes and strummed the three chords I had learned and then sang in a dry, crackly, embarrassed voice:

"I play the banjo better now than him who taught me to

'Cause he plays for all the world and I just play for you."

She laughed and said, "That's good. I like that."

The words would not have made any sense if Mom had not explained their meaning to me.

"Do you get what the words mean?" I asked.

"Sure I do," Angelina said.

"What?" I asked.

"They mean you play the banjo now more than your teacher does because he's busy and you don't have anything else to do." That wasn't quite the way Mom had explained it, but I was too embarrassed to discuss it.

I stood up. "Well, I gotta go now."

"Come back again," she said, and waved to me as I left.

Two weeks later I went with Pop to see Angelina again. She was asleep when we arrived. She didn't sit up, but stayed on her side and looked sleepy even after she woke. Her face was drawn and dry and her eyes were

She said, "Don't pick flowers. Let everything live as long as they can." Much later, I wondered if she knew then what was happening to her.

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very large. Her cheeks were the color of ivory and her thin lips were a pale pink. Her ears looked bigger, and her neck was skinny.

Pop left, "to see other patients," he said. Through the window I could see him go out, get into the car, and begin reading a journal.

"How are you, Angelina?" I asked.

"Fine, I guess. I'm not hungry anymore. I got a present for you. My father did it. I asked him to. It's in a box under the bed."

I reached under the bed and pulled out a cardboard box about a foot square. It was heavy. I put it on the foot of the bed.

"Open it," she said.

I opened it. After removing the excelsior packing, I found a rose carved out of marble. Rising from a base six inches square was a slightly curved stem about the same length, with carved leaves—even little thorns—and at the end of the stem a fully opened delicate wild rose, with distinct petals. I couldn't understand how her father could have carved it.

"It's Carrara marble from Italy," Angelina said.

"That's the prettiest thing I ever saw. I like it a lot. You tell your father."

"That's all right," Angelina said. "I'm glad now."

I put the rose back in the box with its packing. Soon after, Angelina fell asleep, and didn't see me wave to her when I left.

When I got home I went up to my room. I cleared off the top shelf of a bookcase and put the rose all by itself on the shelf where I could see it from my bed.

During the following weeks I asked Pop again and again when I could go with him to see Angelina. His evasive answers: "maybe," "pretty soon," "not just yet," left me wondering why I couldn't see her. But I had no idea what was really happening to her.

One evening, when I was sitting up in bed reading a storybook before going to sleep, Pop came into my room and sat down on the edge of my bed.

"What are you reading, son?" he asked.

"Nothing, Pop. Mostly pictures. When can I see Angelina?"

"Angelina has gone away," he said.

"Where did she go?"

"Angelina died, son. Her blood never got well. She would not have been happy staying here."

"She won't be back, will she?"

"No," Pop said. "You know when people die—just like your colt did when it died—they don't come back. They go somewhere else—wherever God wants them to."

Tears came to my eyes.

"God took her away, didn't He? Is that right?"

"Yes," Pop said.

"I'm mad at God. Why did He do that?"

"He decided that was best for her."

"How does He know?" I asked through my tears.

"Sometimes I wonder," Pop said. "But He knows better than we do. Angelina will always be happy where she is. She will have birds and pets and flowers and music with her to keep her happy."

Pop stood up. "Stretch out and I'll cover you."

I slid down in my bed. Pop pulled the summer blanket up around my neck, kissed me, and went down the hall to his room.

When I heard his door close, I got out of bed, took the carved rose off the shelf, and put it in bed beside me. I said over and over to myself, "Angelina Rose, Angelina Lamb, Angelina Montanelli," until I fell asleep.

In the morning, before breakfast, I ran down to the sheep shed, picked little Angelina Lamb up in my arms and rubbed her nose with mine. □

My father took some blood from her arm. I had never seen this before, and when the syringe filled, I slumped into a chair. Angelina didn't make a sound.

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Guts

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Ato Makere stood looking out from the entrance of the hut which had been home all of his 74 years. At four o'clock the morning sun had not yet arrived, and, almost three miles high in the Ethiopian Simien Mountains, the air was cold. As if suspended on invis-

ible threads close overhead the silvery stars shimmered and danced as the gusts of wind blew through them. The thought came to him that there was no rest for God in the African night—so much fear and pain—so much beginning and end of life.

Wrapping his shama more closely about himself, he walked to the center of the hut. For three days his abdomen had been swelling; the crampy pains had become more severe. He knew he had a "stoppage," for he could no longer retain anything in his stomach.

He approached the thong bed where his wife was asleep, and gently took her hand. She awoke and turned her face toward him. Both her eyes were destroyed by trachoma. He told her he must go now, and she answered, "Da nas da ling" (God go with you). Before letting go of her hand, he pressed it a little more firmly. They understood. She had done all she could.

Three times, with him lying prone across her lap in her eternal darkness, she had irrigated his lower intestine through a bullock horn funnel with a brew made from the leaves of the koska plant. It had not helped. Nor had it helped to cauterize his abdomen with hot coals and beat it with eucalyptus switches. Let the white foreign doctors try now.

In all his years Ato Makere had been no farther from his farm lands than the Debarek Market five miles down the mountain trail. He had heard of the hospital at Gondar, a village of many families, 90 kilometers south. He would walk the entire distance, some of it on paths more than 2,000 years old, and all the way he would know where he was in relation to his home village and his destination.

I was in Gondar as a volunteer visiting surgeon at the hospital, and had been there for only a few months. But even in that short time, I had seen enough so that nothing surprised me.

I saw Ato Makere for the first time about midnight three days after he began his journey. He was standing outside the hospital. He was six feet, four inches tall, and, in spite of his extreme exhaustion and protruding abdomen, he stood straight as a bamboo shoot. His full head of short, cropped, curly hair, his eyebrows, and his contoured beard were silvery white. His clear brown eyes and white teeth gleamed in the night light, and the unwrinkled skin of his face glistened like a freshly opened horse chestnut. There was a majesty and dignity about him that reflected faith in his God, defiance of adversity, and pride in himself and the generations before him.

His problem was obvious. He was suffering from an obstruction due to torsion of his colon—a condition common among Africans and Asians—which would, unless relieved by surgery, eventually lead to gangrene with ensuing perforation, peritonitis, and death. An interpreter explained this to him. After looking into my eyes, and studying intently the backs and palms of my hands, he accepted me.

The hospital dressers completed a few preparations. He insisted on walking to the operating room in a building 75 yards away. With his nasogastric tube thrown over his shoulder, holding high in his right hand the bottle of fluid running into his left arm, and with his catheter flapping between his knees, in the morning light we walked together to the operating room.

Before he was given anesthesia, he sat on the edge of the table, took my hands in his, and, with tears in his eyes, bowed, which in any language could only mean "thank you."

The operative findings were almost unbelievable unless seen. A segment of colon, normally the size of a Polish sausage, had become the size and color of half an inflated black rubber inner tube twisted into a figure eight. Fortunately, the destroyed segment was resectable.

His equanimity and courage were incredible and carried him easily through convalescence during which he never asked for any medication for pain.

On the ninth day in the hospital he demanded that he be released. He said the rains would soon swell the rivers in the gorges, barring him for months from his village. There was much to do on the land, and he also feared the baboon would attack his defenseless wife. I had no arguments as cogent as those why he should stay with us. He held my hand in both of his, bowed again, picked up his stick, and walked out of the compound headed north for his beloved mountains 90 kilometers away. □

I first saw Ato Makere after his 90-kilometer walk to the hospital. In spite of his extreme exhaustion and protruding abdomen, he stood straight as a bamboo shoot, his majesty and dignity reflecting faith, pride, and defiance of adversity.

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Madness, Medicine, and Justice.

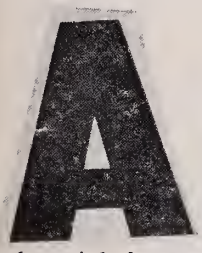
A Cross-Examination of the Insanity Defense

by Thomas G. Gutheil

Particularly since John Hinkley was acquitted of shooting President Reagan, the insanity defense has been the subject of intense controversy. Why does society allow such a defense, and what role should psychiatrists play in it?

Thomas G. Gutheil '67 addressed these and other questions in an informal talk at the Beth Israel Hospital in April. "Today's presentation is intended not to make lawyers of you, but to present clinical issues and considerations that bear on this complicated and important subject," he told his audience of hospital staff. This article is an adaptation of that talk, and the New Yorker *cartoon reproduced in these pages is one of those Gutheil used to illustrate it.*

Gutheil is director of the Program of Psychiatry and Law at Massachusetts Mental Health Center and associate professor of psychiatry at HMS. He is co-author, with Paul S. Appelbaum '76, of Clinical Handbook of Psychiatry and the Law.



lthough the insanity defense has been a hot issue in recent times, it is a widely misunderstood subject. After the Hinkley trial, for example, Russell Baker wrote an Observer column called "Shrinking from Justice," in which he makes four out of the four possible major misperceptions of the insanity defense. Now, Russell Baker is no fool, yet so powerful and pervasive are these misperceptions that even someone as intelligent and alert as he can fall prey to them.

Baker's first error reads: "When insanity is the question at law, psychiatrists almost always split down the middle like this, which makes you wonder about the state of the psychiatric art. If psychiatrists can't agree about whether you're a lunatic or not, then who can?"

Here Baker misses the critical point that the judicial system is based on an adversary procedure. One side wins; the other side loses. The defense "disagrees" with the prosecution 100 percent of the time, yet we do not conclude that the law doesn't "know" who is guilty. The task of the psychiatrist on one side is to pull out those psychiatric factors in the patient's clinical state at the time of the event that might make a case for sanity, while the psychiatrist on the other side pulls out those factors that might make a case for insanity. Both present their cases to the jury, and the jury weighs and balances, and decides which it believes. Therefore, it's not that "psychiatry almost always splits down the middle"; it's that, in a courtroom setting, psychiatry always *must* split down the middle, because if there isn't an expert on both sides, in theory, then the jury isn't getting a clear adversarial picture.

The issue is the credibility of a witness versus that of a profession. One engineer should testify that the falling of a bridge was an accident, another that it was negligence. Yet nobody would say that engineering is weakened as a science.

Ideally, because there's room for disagreement in all complicated cases, it should be possible to get two equally qualified professionals to make cases for the two sides. Unfortunately, as I have discovered in my own courtroom experiences, all too often on one side there is a psychiatrist who gives a considered opinion, but on the other a psychiatrist who will say whatever the attorney wants—a "hired gun." Perhaps the emergence of more forensic psychiatrists able to bring out the relevant features will help solve this problem.

The issue here is the credibility of a witness versus that of a profession. If a case concerns a bridge that has fallen down, there should be an engineer who says, "The falling of that bridge was an act of God, unforeseeable by mortal man. Accident." And there should be another engineer who says, "These are the facts that make the falling of that bridge an example of clear negligence on the part of the Negligent Construction Company, Inc." The engineers *must* "disagree" if the trial is to be fair, yet nobody would say that engineering is therefore weakened as a science.

Baker's second error: "If the scientific authorities on insanity can't agree, why does the law assume that an assortment of clerks, housewives, and mechanics can supply the correct answer?" Psychiatrists are not scientific authorities on insanity; we are scientific authorities on mental illness. Insanity is a legal, not a clinical concept; it defines a mental illness in particular circumstances that is specific enough in focus to be exculpatory for an alleged criminal act. Despite Baker's patronizing dismissal, it is precisely the jury that *is* "expert" on insanity.

The third error: "In any case, what difference does it make? A shot president is just as shot, regardless of whether his attacker is insane or not." Here again Baker misses the key point. Is this statement true or false: "Shooting a president is always a crime"? Consider: if an attacker lunges at the president with a knife and a security guard shoots at the attacker but accidentally shoots the president, it's an accident, not a crime. Or, God forbid the occurrence of this unlikely scenario, in which shooting a president could be self-defense: "The president came at me with a knife. What was I gonna do? I had to shoot him." Distinguishing accident from negligence or intention is a central issue in the law, and intent is crucial in the decision of whether a given act is a crime.

Finally, Baker's fourth error: "Surely the legal system is going to keep the attacker off the streets for a long spell no matter what his mental state at the time of the crime." The dispositional question is what most people are really worried about: "Am I in danger because Hinkley is walking the streets?" (I would cheerfully predict, by the way, that only two people,

Jodi Foster and Ronald Reagan, are directly endangered by John Hinkley. The rest of us don't matter enough to him to be endangered by him.)

The concern about disposition reflects a popular misconception of the insanity defense that is one of the hardest to eradicate: that millions of felons are pouring back into society through this giant loophole in the law. Actually, only a tiny percentage of defendants try it. It's a defense of desperate cases, such as Hinkley's, when the act has been videotaped and there really is no other defense.

Of the few who apply, only a small proportion are found not guilty by reason of insanity, because juries tend not to like the defense. In fact, perhaps nobody really likes it, but the law is wedded to it as an important part of the jurisprudential system.

Why, then, do we have an insanity defense? I believe the credibility of the judicial system is as important as its data base. The judicial system would be viewed as fundamentally flawed, and people would experience a basic personal and social revulsion against it, if some individuals were treated as responsible when they were obviously not. It would weaken the perception of fairness of the entire system.

In recent times, psychiatry has been caught in the crossfires of changing social attitudes. Over the years, the libertarian bar has been making it tougher and tougher to put or keep anyone in a hospital. But that movement, left over from the '60s, has clashed with the rightward shift of the rest of society. An off-the-streets mentality prevails now: "I don't care if they're sane or insane, get 'em off the streets."

It usually takes the courts three to 10 years to catch up with social drifts, so I predict that we will see many cases that reward conservative, off-the-streets practice—hospitalization—whereas before, the courts were very interested in springing large numbers of people from institutions.

The legal definition of "insane" has also varied widely in accordance with social attitudes. The pendulum swung to an extreme in 1962, in a sweeping definition from the case *U.S.* v. *McDonald*: "Mental disease or defect ["disease" usually means mental illness; "defect" usually means retardation] includes any abnormal condition of mind which substantially affects mental or emotional processes or substantially impairs behavioral controls." That test is so broad, on Monday mornings *I* probably qualify for it; perhaps we all can remember times when we couldn't pass it. After swinging to that all-encompassing extreme, the pendulum is now swinging the other way.

Psychiatrists are not scientific authorities on insanity; we are scientific authorities on mental illness.

One reason the public is so confused about the insanity defense is that the definition of insanity differs from state to state. The rule in most jurisdictions, however, stems from at least one of the three most famous tests for insanity.

The first of these is the *M'Naghten* test, which is still the rule in some jurisdictions in the United States. It

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originated in England in 1843, after a man named Daniel M'Naghten experienced a delusion that the bad guys in Parliament were ruining him through diddling with the Corn Laws. To express his dissatisfaction, he attempted to shoot Prime Minister Peel, but instead hit Peel's secretary, Drummond, whom he had mistaken for Peel.

M'Naghten, who was probably fairly crazy, was found not guilty by reason of insanity. There was a tremendous public outcry against the verdict, an outcry which was expressed even by Queen Victoria. The judges, responding to questions from the House of Lords, presented what is now the *M'Naghten* test: "A person is not responsible if, by virtue of mental illness or mental defect, he is unable to know the nature and consequences of his action, or if he does know it, to know that it was wrong."

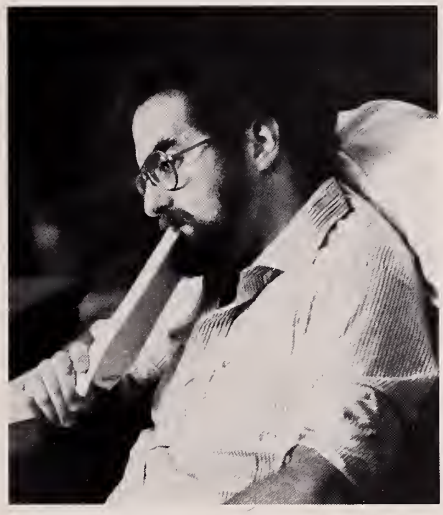
M'Naghten is a two-pillar test, with a knowledge component and a wrongfulness component, which reflects in part the 19th-century view that parts of the mind existed in discrete compartments. According to this view, you could know an action on one hand, and know it was wrong on the other.

"Wrong" has always posed a problem. Does "wrong" mean unlawful or immoral? For example, someone says, "Killing is wrong, but my landlord was clearly an agent of the devil sent to tempt me to thoughts of sex. So killing was too good for him. But killing in general, of course, is a sin and decried by God." The question of immoral versus unlawful wrong persists in many of the other tests.

The next important test was the *Durham*, or product, test of the 1950s: the defendant is exculpated if the alleged act is a product of mental illness. In theory, anything that might bear upon the final common pathway of behavior can be exculpatory. But, of course, that definition raises as many problems as it solves. Causality is always complex. According to the principles of overdetermination and multiple function, everyone's actions are the final common pathway of an immense web of associations, intentions, and experiences.

It isn't clear what role the unconscious is supposed to play in this test. And does "product" mean the inclusive product—including a large number of factors—or the exclusive product? In other words, does the illness have to have led *directly* to the action (not passing Go, not collecting $200), or can there be other ways in which the illness and action are linked up?

If you don't know who the victim is, if you don't know who you are, if what's going on is a complete mystery to you, that would seem to have some powerful impact on your intentionality.



Thomas Gutheil

The latest test emerged when a group of law scholars and professors known as the American Law Institute (ALI) put together the Model Penal Code, now the rule in most jurisdictions. Part of it addresses the insanity defense. Another two-pillar test, it dictates that a person is not responsible if, because of mental disease or defect, he lacks substantial capacity to appreciate the wrongfulness of his actions, or if he is substantially unable to conform his conduct to the requirements of the law.

Because this test has become the most important, let's put it under the microscope. First, "mental disease or defect" means there has to be an official mental disease. People who are simply out of control for other reasons, in theory at least, aren't eligible. Obviously, there is room for debate about whether certain conditions, such as psychopathy, are diseases.

In the phrase "lacks substantial capacity," the word "substantial" is an attempt to be quantitative, which the law likes to be. But psychiatrists do not usually quantify most of their assessments and decisions. So the question of how much is "substantial" is decided by the judge or jury.

The word "appreciate" is designed to include affect, a factor the *M'Naghten* and *Durham* tests ignore. Manics, for example, are cognitively aware of their limitations, but their grandiose attitude and affect impair their ability to grasp the emotional dimension of their actions.

"Wrongfulness" poses the same problems as in the *M'Naghten* test.

"Able to conform" raises the question of *unable* versus *unwilling*. Of course, there are levels of ability: some people, under certain circumstances, are more vulnerable to giving in to their impulses than others.

So the ALI test has a cognitive, an affective, and a behavioral component.

As originally written, the ALI test had a very important exclusionary phrase to the effect that mental disease or defect is not necessarily demonstrated by the repeat offender. Forensic psychiatrists refer to this phrase as the psychopath exclusion. It is an attempt to avoid the shortcut reasoning that would conclude: anybody who has been in jail this often must have something wrong with him or her. Some state legislatures don't include this phrase, so the jury must decide case by case if psychopaths qualify; in other states, the entire ALI

PHOTO BY BILL O'CONNELL

test has been incorporated.

Two other closely related tests for insanity, "irresistible impulse" and "extreme emotional disturbance," are valid in a few states. The first raises the question of the distinction between irresistible and unresisted impulses. How powerful do impulses have to be before you can say that they are beyond your power to resist? Frequently this test and the *M'Naghten* test are used jointly.

The extreme emotional disturbance (EED) test is the legal system's way of incorporating a fundamental social sense of the difference among certain crimes. Here's an example of a case in which EED might apply: A robber comes into a mom-and-pop grocery store. In the hold-up, he shoots the mom. Pop goes upstairs, calmly loads his gun, and comes back and shoots the perpetrator. Those crimes are perhaps equivalent, but our moral sense is offended by the crime in the first instance, and is somewhat more ambivalent, or maybe even exculpatory, for the second. We assume that something different is going on in the mind of the pop than in the mind of the hold-up man.

The average, garden-variety family murderer probably cannot murder without some alteration of the state of consciousness. But if all these murderers qualify as insane, then nobody is guilty.

The accompanying table presents a non-exhaustive list of the areas in which I think psychiatrists have something to offer concerning the insanity defense. These are the areas of intact functioning that someone should have in order to be considered responsible. Or, to put it the other way, impairment in any of these four areas could influence intentionality. These are not the legal but the clinical or psychologic elements.

Reality. It seems to me that in order to have intention, you have to have some sense of reality. If you don't know who the victim is, if you don't know who you are, if what's going on is a complete mystery to you, that would seem to have some powerful impact on your intentionality in relation to the given act.

What impinges on the sense of reality? Obviously, the psychoses. We can informally divide the psychoses into four areas: perceptual, in which you miss the reality by disorders of perception; cognitive, in which you have delusional beliefs, you don't quite grasp what is going on or you misinterpret what you see; the affective psychoses, which color your sense of what's real by an affective influence, as in mania and depression; and misidentification syndromes, the belief that one's family has been replaced by impostors, that one is not oneself but someone else, and so on.

Apart from the psychoses, dissociative states impinge on the sense of reality, and they raise a special problem. As you probably know, the majority of murders occur in the family; murder by a stranger is a rarer event. The professional hit man, assassin, or spy may be able to kill without being in a dissociative state, but the average, garden-variety family murderer probably cannot murder without some alteration of the state of consciousness. If all these murders occur in some slight state of altered mentation that qualifies for insanity, though, then nobody is guilty. I bring that up because it presses upon the rule and shows the dilemma.

Post-traumatic stress disorder may affect a sense of reality. Consider this example: the combat veteran is having a flashback experience, reliving combat. Somebody taps him on the shoulder, and—because he's momentarily back in the jungle in his mind and he's being tapped when there shouldn't be anyone there—he instinctively strikes out and kills or injures. We might well say that the reality sense here is sufficiently altered to raise questions about intent.

Mens Rea Impairment by Clinical Entities

1. Reality
Psychoses
- Perceptual
- Cognitive
- Affective

Misidentification Syndromes
Dissociative States (P.T.S.D.)

2. Causality/Consequences
Mental Retardation
Judgment-Impairing Factors
- Deliria
- Intoxications
- Senile Changes

Dissociative States

3. Intention/Will
Deliria and Toxic States
Obsessive-Compulsive Neurosis
Influence Delusions
Dissociative States

4. Mind/Body
Seizures and Related Dissociative States (Rage Reactions, P.T.S.D.)

Causality and consequences. You have to know what the consequences of your action are going to be in order to be held legitimately responsible. Retardation obviously impairs such recognition, as does anything that affects abstract thinking. Deliria, intoxication (particularly from PCP and alcohol), senile changes, and dissociative states all can interfere with the sense of what will happen as a result of one's actions.

Intention and will. Diseases of will, which impact directly on *mens rea* (a legal term meaning guilty mind, criminal mind, or criminal intent), include delirium, toxic states, obsessive-compulsive neurosis (rarely associated with crime), delusions of influence ("the devil made me do it"), and, once again, dissociative states.

Mind-body problems. These problems include temporal lobe complex partial seizures, certain phenomena called rage reactions or episodic dyscontrol, and, again, post-traumatic stress disorders. These disorders may impinge at the mind-body connection and produce impairments that potentially qualify for the insanity defense.

Now let's turn to some of the practical difficulties in the insanity defense. One problem is that psychiatrists in a treatment setting are accustomed to seeing the world through the patient's eyes. They attempt to achieve an empathic, "patientocentric" view of the world. In a forensic setting, the psychiatrist must assess the entire situation, which includes the views of the perpetrator, the witnesses, the arresting officer, the victims if alive, and so on. Psychiatrists have to shift gears into a completely skeptical and objective or even disbelieving view—suspending their empathic skills to some degree. That doesn't mean that they shouldn't listen empathically to the patient, or defendant in this case, but it does mean that they have to be able to go beyond empathy and to understand the power of self-serving forces in such an assessment.

In a forensic setting, psychiatrists have to shift gears from an empathic, "patientocentric" view to a completely skeptical and objective or even disbelieving view.

Second, a tremendous amount of time often elapses between the act and examination: the case may come to trial years after the original event. In that time, the memories of the patient and witnesses can alter. Most of us can't remember precisely what happened last Friday. Even something that makes as powerful an emotional impact as a crime can be forgotten over years.

The most important issue is the alteration in clinical state. Inevitably, the insanity assessment is a retrospective view. The patient, examined even days after the fact, may be in a completely different clinical state from the time of the alleged crime. This change is very important, because it causes juries much distress. The jurors in the courtroom today are looking at a rational, quiet, often treated individual, and they are hearing about a raving lunatic who allegedly committed the past crime. The jurors have to use their imaginations to get into the person's mind at the time of the crime.

Next, the fate of the defendant is a very powerful factor. In a simulated trial I participated in with Arthur Miller on "Miller's Court," as I recall, the jurors had no interest at all in the views of the witnesses. They were arguing about whether to let the defendant back onto the street. They had immediately shifted gears to the dispositional question, as Russell Baker did.

Last, there's the problem of the sociopath. Neither psychiatry nor the criminal justice system has ever really known what to do about the sociopath. I think we need to accept that reality and then decide as a society what we want to do about it.

I'll conclude with an update of some late developments. The ALI test, you recall, has an appreciation component and a conforming-behavior component. Both the American Psychiatric Association (APA) and the American Bar Association recommend simply removing the behavioral component, so that we do not bog down in the essentially moral question of which impulses are irresistible and which are unresisted. The determining issue then becomes whether the individual appreciated the wrongfulness of what he or she was doing.

The APA has specifically recommended that the insanity defense be reserved for serious illnesses, like psychoses, such that "insane" would mean approximately what the average person on the street thinks of as "crazy"—not subtle personality disorders, but flagrant aberration. Psychiatrists should then be able to testify to the clinical material at issue—to "do psychiatry," as the APA statement on the insanity defense puts it.

The APA and the ABA also recommend that we as a society continue to have an insanity defense. We should keep the plea of "not guilty by reason of insanity," and *not* choose alternatives like "guilty but mentally ill" or "guilty but insane," as has been suggested. Among other goals, this approach would force juries to grapple directly with the frankly moral question of guilt versus exculpation.

We haven't heard the last of these issues: even now some attempted remedies will soon be translated into legislation. The insanity defense may always represent an area where strong feeling defeats the exercise of reason. My hope is that the underlying issue, namely the perception of fairness of the judicial system, is candidly and fairly addressed, since the psychiatric role is clearly secondary to this fundamental question. □

Five Poems

by Michael Stewart '65

No Time, No Words

there is no time
for reconsidering the past,
for recreating what was lost,
for retroactive grace....

there are no words
interpreting what senses find
unravelling the facts at hand
resolving the absurd....

there is no way
to salvage time
to fashion words
to mimic Truth—
which mocks our words
and in its time
finds ways....

Biopsy

where does it hurt
where
was it that you felt
an ache
an emptiness
(between too solid flesh)
a never-guessed (too late
to be dismissed)
untidiness
a vacant knot
to be denied

yesofcourse
we can
will
did what
we did without
a moment's hesitation

and now
where does it hurt

Michael Stewart's obituary appears in this issue.

I Told A Friend

one day (a fragment
torn from other times
which memory never mended)
i told a friend:

life is all
about-face.
what starts is never
ended.
what lies
beneath today's truth
can never be
surrendered.
suffer it with grace.

and then i wondered:
could grace be
comprehended?

Renewal

What blossoms, new each day,
Unfold their fragrance
In the corners of my heart,
And will not die?

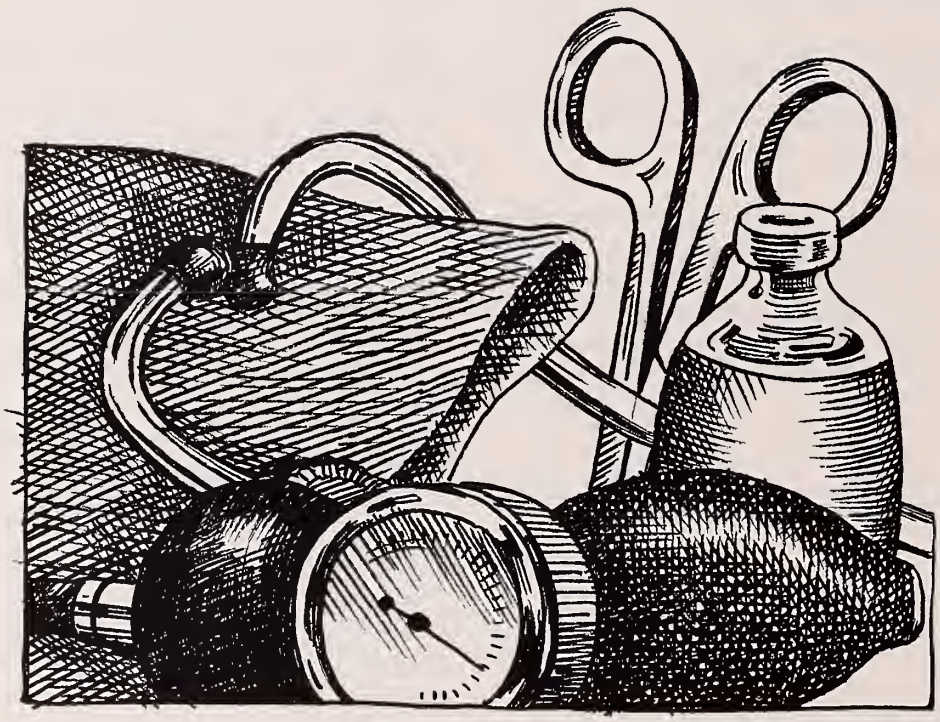
What strange and secret petals fall
To nourish withered roots,
And fashion under me
A cushion for my unbelief?
From which I watch, and reach,
And touch the magic flowers....

First-Born

two infant eyes, feeling
this way,
and that,
explore the unsure silhouettes,
secured merely
by an inconclusive focus

two eyes light
a mother's face,
compounding greed with innocence,
and grace a father's,
puffed and proud, a little
blurred around the edges

eyes and faces, joined
to play new games by ancient rules,
extol a common heritage
until
they weary of each other's eyes and faces
turning to find comfort
in their separate shadows,
partners
in a fleeting recognition



Holistic Medicine: Fringe or Frontier?

Explorations Beyond the Biomedical Model

by James S. Gordon

HOLISTIC MEDICINE. TO SOME, the words are offensive: the adjective seems to profane the noun. Others reserve wry derision for its practitioners, for the curious and unconventional therapies they may prescribe. Some embrace holism as if it were messianic, embodying all that is innovative and redemptive. And still others, perhaps the vast majority, are puzzled. What is holism? Is it new or old, revolutionary or redundant? What does it actually contribute to the day-to-day practice of medicine? And why are so many people involved in it, or at least intrigued by it?

The concept was first popularized by South African statesman Jan Christian Smuts (perhaps better known in his military and political capacity) in his 1926 book *Holism and Evolution*. To Smuts, holism was a way of comprehending and describing organisms and systems as entities greater than and different from the sum of their parts, a corrective to the analytic reductionism of the prevailing sciences.

In the last decade, the word "holistic," and its Anglicized cousin, "wholistic," has been revived and applied—and misapplied—to almost every human endeavor, from primary education to jogging to home building. Perhaps its most fertile ground has been in medicine and health care—in part because its principles have always been integral to healing. Hippocrates, for example, emphasized the environmental causes and treatment of illness, and the importance of emotional factors and nutrition.

We are also now realizing, as microbiologist Rene Dubos suggested in *Mirage of Health*, in 1959, that there are inherent limitations to the technological advances which have proved invaluable in treating acute illness, and have helped cure or cor-

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ILLUSTRATION BY KATHERINE MAHONEY

rect infectious diseases, vitamin deficiencies, and congenital defects. Such advances have been unable to stem the tide of "mental" and environmentally related illnesses — including hypertension, diabetes, obesity, cancer, depression, and alcoholism — which have in the last half-century become the chief agents of our mortality and morbidity. For both patients and providers of care, there are difficult side effects — economic, interpersonal, and biological — of unnecessary diagnostic and surgical procedures, over-medication, and an impersonal, fragmented system of care.

Whatever the present shortcomings of holistic medicine — and I will discuss some of them later — its ideal represents an antidote to the narrowness of specialization, a fresh attempt to understand and treat whole people in their total environment. Without neglecting the treatment of disease, it includes an appreciation of patients as mental and emotional, social and spiritual, as well as biological and psychological beings. It emphasizes approaches — diet, exercise and massage, introspection, biofeedback, and attitudinal change — which respect the patients' capability for healing themselves.

My own journey toward holism, or, more precisely, my discovery of the holistic tradition in medicine, has been quite personal and circuitous.

When I graduated from Harvard Medical School in 1967, most of my classmates and I moved confidently forward into our specialty and subspecialty training, focusing on the latest physiological or pharmacological advances in our particular area of interest. Some kept a hand in basic research, or admired colleagues who did. Even those of us who gave primacy to the "humanistic" aspects of health care suspected the real frontiers of medicine lay with the painstaking explorations of the biomedical scientist.

I was, if not typical, at least on the bell curve for that year's aspiring psychiatrists. I had considered becoming a surgeon like my father, or a general practitioner like my grandfather. I liked the idea of taking care of whole families over many years. But my real pleasure, I discovered, was in talking to people, in exploring their inner worlds, in understanding and helping them to understand the connections between their life histories and illnesses. I had worked on the wards at Massachusetts Mental Health Center, and, in my senior elective, with autistic and schizophrenic children.

By the time graduation came, I was prepared to believe there was an important distinction between physical and mental illness. The former, though influenced by emotions, was basically physiological, appropriate for definition and treatment according to a biomedical model. "Mental" illness (I began to consider this an inappropriate metaphor), with such obvious exceptions as phenylketonurea, pellagra, and perhaps autism, was basically psychological and social.

Over the next 10 years I explored the possibilities of psychosocial treatment in and outside of mental hospitals. I grew to believe that medication, particularly in an institutional setting, was often used as a tool for foreclosing, under the aegis of therapy, ideas and behavior which were unconventional and disturbing to the staff. As a chief resident at Albert Einstein College of Medicine, I created with my coworkers a safe setting for psychotic people to re-experience, so they could reintegrate, fragments of early experience and fantasy — a place for what Scots psychiatrist R.D. Laing had called "the natural healing process of madness."

Later, in the community psychiatry laboratory of the National Institute of Mental Health, I worked with non-professionals to create supportive settings — hotlines, runaway houses, and group foster homes — for troubled and troubling young people.

I became fascinated by the way different social and attitudinal settings seemed to affect the very nature of our patients' "mental" illness. "Everywhere else," one chronic schizophrenic young man remarked, "I'm crazy. But here I'm sane."

Our refusal to emphasize psychopathology with these young people, and our insistence on their strengths, seemed to change how they felt about themselves. Parents who came to the runaway houses often marveled that the surly, rebellious, spaced-out kid who had always resisted the therapy they had suggested, was now cleaning his room, hauling out the garbage, and insisting on family counseling.

When I wasn't working with these community-based services, writing about them, or, later, directing NIMH's work with them, I was seeing private patients. My professional life seemed very much in order. There was a satisfying continuum stretching from the dynamic interpersonal psychotherapy I practiced with individuals and families in my private practice, to my attempts to alleviate "mental" illness by changing the settings and attitudes of therapy and therapists, to my concern with larger institutional and social change. People were respectfully reading what I was writing. I was becoming an expert.

Yet something was beginning to nag at me. It was obvious that just as psychological factors could affect physical health, so biological factors could affect psychosocial functioning. What really bothered me, I realized, was the reductionist way we viewed biology itself, and the biological therapies we had developed to treat aspects of "mental" illness. Too often such treatments seemed to violate thoughts and feelings of our patients, or relieved one set of biological problems only to create others.

Perhaps one could view biological symptoms, like psychological symptoms, as clues to the origins of the disturbance, as opportunities for growth and change. Perhaps patients could, with our help, apply an introspective approach to their disturbance and its origins, and could discover and use nontoxic remedies.

I cast about for answers to my questions, and discovered excerpts from Chinese scientific journals, which I found hard to believe, about the successful and widespread use of acupuncture analgesia in major surgery, and the relatively successful treatment by acupuncture of anxiety, schizophrenia, osteoarthritis, and bronchial asthma. There was no apparent anatomical reality to the channels or "meridians" which were presumed to run beneath the skin, no reason I could puzzle out that a needle placed in the foot would improve liver functioning.

At first I thought the successes of acupuncture might be placebo responses: the combination of the patients' positive expectations and their esteem for the practitioners in a sup-

portive social context. But the technique had been used by hundreds of millions of people for several thousand years. There must be more to it.

Then I read that acupuncture was being successfully used in veterinary medicine. Either the Chinese scientists were lying, or.... Something shifted in my mind; my narrowness and chauvinism dropped away, at least for the moment. Here was an apparently effective healing practice based on premises quite different from our own, one which conceptualized the physical and mental as two aspects of an embracing "energy" system, a practice which brought the same, apparently non-toxic, techniques to bear on treating both.

At about the time I was beginning to read about acupuncture, a series of events brought one of its practitioners, an osteopath named Shyam Singha, to my house for a three-day visit. He was unlike any physician I had ever known, as strange and fascinating as the root workers and brujos I had briefly met in ghettos and barrios, or the shamans I had read about in the pages of Eliade, Lévi-Strauss, and Castaneda.

Dr. Singha's discussions of Oriental medicine, of the balance between Yin (negative) and Yang (positive) energy and the Law of Five Elements, seemed by turns brilliant and absurdly fanciful, more like religious belief than medical fact. I didn't trust half of what he said, but just when I was about to dismiss him as a charismatic quack, he connected physiological functioning to acupuncture principles, or quoted the relevant articles from the Chinese, and even the British, medical literature. I knew he knew something I didn't.

A year or two after I began to reconsider my attitude toward the biomedical model, six months after I met Dr. Singha, in the middle of my tentative explorations of Chinese medicine, I injured my lower back. I had pains in the lumbosacral area, and numbness and paresthesias in my left leg and foot. I was bent almost double.

I consulted the orthopedic surgeons at Bethesda Naval Hospital (I was in the Public Health Service), who prescribed bed rest, muscle relaxants, and a heating pad, and deferred their diagnosis.

I stayed in bed, bemused and nonfunctional from the muscle relaxants, and arose two weeks later little better. When I returned to Bethesda I was told that I might, indeed *should*, have back pain, but couldn't possibly have the symptoms I detailed unless I had a disc problem—and, so far as they were concerned, I only had lumbosacral strain.

It now seems to me that the most therapeutic attitude for physician and patient alike is one which regards illness as an opportunity for personal growth—and the physician as a catalyst and guide.

I began to think, with, I confess, far greater sympathy than before, about all the patients who had described vague symptoms which fit no known syndrome for whom neither I nor other doctors could do anything.

For about two months I did the prescribed back exercises, and rested when told to. Then, only marginally better and quite impatient, I turned to the highly recommended chief of orthopedics at one of the city's major teaching hospitals. He reviewed my x-rays, expressed concern, mentioned a myelogram, but offered no answers, no help.

Finally I decided, at a friend's urging, to see a local osteopath. The idea made me exceedingly nervous. It was one thing, I realized, to learn the theory of another medical system, or even to talk to a curious, maddening, and perhaps mad, fringe practitioner like Shyam Singha. It was quite another to submit my own body—a body used to the most scientific and sophisticated Western medicine—to one of its adherents.

The osteopath I consulted announced I had a "lesion" in my back, that the lumbar vertebrae were pressing on the nerve roots as they emerged from the spinal cord, and that he could do something about it. He put me on my side, one leg dangling from the examining table, and "manipulated" my back.

The crunch I heard as he leaned hard on my hip conjured dreadful visions—discs extruding, paralysis, and impending impotence.

Within minutes I was standing—not bending over, but actually standing. The numbness and tingling were receding. I was ecstatic, until, five minutes later, the pain and paresthesias returned. Still, I was hopeful: something had happened, even if it had lasted only briefly. I returned a few times, but the results were similar. Finally, close to despair, just before I was to submit to a myelogram, I called Dr. Singha in London.

Stop the medication, he said. Take hot baths with Epsom salts and then cold showers. Eat three pineapples a day for a week and nothing else.

I thought the trans-Atlantic phone had gone bad. He repeated his prescription. I could hear what sounded like the roar of the ocean in the line while I stood with my mouth open.

"Why?"

"It won't make sense to you."

"Why?"

"Pineapple has malic acid."

"Yes, I understand that." (I am impatient.)

"Malic acid affects the lung and colon." (He is fast losing credibility.) "In Chinese medicine the lung and colon are the mother of kidney and bladder." (The mother?) "The bladder and kidney are connected to the back. . . ."

He was right. It made no sense. But I didn't want the myelogram, and I didn't want surgery, and something about Dr. Singha, an authority I did not understand, moved me. I decided to do it. I was desperate.

I took my baths and showers, and, to my own amazement, and the amusement of my friends and colleagues, I ate my pineapple. After three days, I called London. "My mouth," I reported, "is full of sores and I have 103 degree fever. My back hurts as badly and the paresthesias are as prominent as when I first injured it."

"For the sores," he said, "coat your pineapple with honey. So far as the rest goes, it is very good. In Chinese medicine, a chronic disease must be made acute before it can be healed."

At first I assumed that in my feverish delirium I had misunderstood. Then, suddenly, for the first time some piece of the treatment made sense to me. In psychotherapy, one often has to relive painful traumatic experiences in the process of

recovery from a chronic debilitating way of thinking or feeling. Perhaps, I thought, the healing of my body was proceeding in a similar way.

At the end of the week I went back to my osteopath. This time the adjustment held.

My mild curiosity about alternative healing techniques now became a kind of fascination. Perhaps the principle of making the chronic acute could be applied to the biological treatment of "mental" as well as physical illness. Perhaps techniques that had been disparaged or ignored in my training could be of use to me and my patients. It was certainly worth some time.

I read about other approaches to health and illness: osteopathy, chiropractic, homeopathy, nutrition and herbalism, relaxation therapies, autogenics and hypnosis, massage, and Rolfing.

I experimented on myself. Over time, I discovered tools—meditation, yoga, Tai Chi (a Chinese moving meditation)—which helped me experience from the inside organs I had once palpated in surgery, and become aware of physiological processes I had seen recorded on laboratory instruments. I discovered that, by sitting quietly and concentrating on my breathing, I could raise the temperature in my fingers, relax my muscles, still my mind. Bending forward and back, moving from one yoga asana to another, I could feel the individual vertebrae form the curves of my spine.

Each time I had an ache, a pain, or an illness, I tried something new. I began to ask myself what I was anxious about, or why I had been careless: What was in it for me to be sick now? I let the images or the words come: "You don't really feel like going to work but don't feel right about missing a day; Your voice is hoarse because there's something you want to say but are holding back." Unresolved conflicts, it seemed, were often the necessary if not the sufficient cause of my ailments.

For a headache, instead of taking aspirin I now tried to use a relaxation technique or imagery—watching in my mind's eye as the muscles in my neck and scalp softened and lengthened. I used herbal teas for sleeplessness and diarrhea, and acupressure,

Teaching massage to patients who are friends with one another.

PHOTOGRAPH BY MARCELO MONTECINO

not antihistamines, for allergies. My treatments were by no means always successful, and rarely was relief as swift as from allopathic medicine. But I was learning from my illnesses—about myself as well as alternative therapies—and I knew I wasn't creating any new problems with my treatment.

I spent several months in England with Dr. Singha learning the fundamentals of acupuncture and osteopathy. In the U.S. I attended lectures and workshops, and consulted the practitioners of different therapies who seemed most knowledgeable and responsible. Sometimes I was sorry: there certainly are a number of incompetent and venal people flourishing at the fringe of medical orthodoxy, feeding on frustration and despair. At other times, I was impressed.

The more I learned, the more curious my previous ignorance seemed. Why had our training omitted musculoskeletal manipulation? It had apparently been part of all the world's healing traditions, and clearly could work to alter peripheral function, perhaps even to modify the feedback loops to the central nervous system.

In my psychiatric training, hypnosis had been dismissed as fraught with authoritarian possibilities, capable only of producing symptom substitution. As I came to understand more about it—and the relaxation techniques to which it was related—I began to see its potential for treating physical as well as psychological problems. I realized that trance states were not unlike those I had entered on the psychoanalyst's couch, that hypnotic suggestions, like the analyst's interpretations, could permit access to memories, thoughts, feelings, and images which might relieve pain, improve functioning, or help resolve psychological dilemmas.

And what about nutrition? I could remember only a few lectures on severe dietary deficiency diseases—scurvy, rickets, pellagra—which we were unlikely to encounter in the United States. Yet it was clear, once I began to pay attention, that how much and what kinds of food I ate affected my mental and physical state.

After awhile, some friends began to ask for help with nagging debili-

Family therapy: the children draw pictures to help explain the "monsters" that haunt their bedroom at night.

tating problems unrelieved by their primary care physician or specialists, problems such as back pain, sinusitis, vaginitis, arthritis, insomnia, and pre-menstrual tension. I agreed to help, but was apprehensive, partly because I had had no formal medical training since internship, partly because there was no body of research, and no articles in refereed journals, to justify my treatments.

I made sure all of my patients had had a thorough, and thoroughly orthodox, medical work-up before they saw me, and comforted myself with the fact that I would in any case be doing them no harm. Finally I decided that I would put all financial incentives on their side—by treating my new patients without charge.

Some of my first patients got better, much better. Some whose physical symptoms didn't disappear still felt better. The success could have been due to specific techniques I used, but I knew it might have been a result of my relationship with my patients and their confidence in me. I couldn't rule out the possibility of a Hawthorn effect—a difference, any difference, making the difference. Still, something useful was happening.

I found that studies on the therapies I was learning were—and still are—not good. There were a few reports from the Soviet Union on fasting, anecdotal accounts on the effects on mood of food, food allergies, and acupuncture, and a few papers on jogging and depression.

I did find much better studies that expanded my view of the interrelationship between physical, psychological, and social well being—and of the role of the doctor/patient relationship in the treatment of physical as well as "mental" illness. A number of recent works have explored the implications of Hans Selye's decades-old research into the psycho-physiology of stress, and have provided evidence to substantiate and extend the clinical descriptions of such pioneers in psychosomatic disorders as Franz Alexander, Helen Flanders Dunbar, Willhelm Reich, and George Engel. Studies indicate, for example, that people who have recently experienced significant loss, particularly those who are not close to their parents, are more likely to develop a variety of chronic diseases than matched controls.

Salvador Minuchin and his coworkers have shown a clear relationship between the free fatty-acid levels of diabetic children and their parents' interactions. Harvey Brenner's epidemiological work has demonstrated a relationship between fluctuations in our national economy and the incidence of a variety of disease conditions. And Arthur Kleinman, Leon Eisenberg, and Byron Good have described how successful treatment of even the most discrete clinical entity can be frustrated by ignorance of the familial and cultural context in which it occurs.

For several years I kept my practices separate: psychotherapy for people with emotional problems, my free clinic and the alternative therapies for those with physical problems that had been refractory to conventional treatment. However, the more patients I saw, and the more I learned about the healing systems of other cultures—all of which I was also investigating at NIMH—the less it it made sense to make sharp distinctions between physical and psychological or indeed spiritual, familial, or social problems.

For a few years, I proceeded tentatively, trying first one therapy, then another. Over time I developed a more comprehensive approach, based on my training in psychiatry and psychosomatic medicine, on Chinese conceptions of balance and change, and on my steadily increasing knowledge of the effects of food and exercise, attitude, relaxation, and meditation on physical and emotional health.

By the late '70s, the term "psychiatry" didn't cover all I was doing, either in my own practice, or at St. Elizabeths, the federal mental hospital where I had become chief of the Adolescent Service as part of my NIMH work. There I was teaching barely literate, periodically psychotic inner-city teenagers to appreciate the connection between what they ate and how they felt, and helping them shape and control their anger and violence not only by expressing and exploring it verbally, but also with relaxation exercises and Kung Fu practice.

It now seems to me that the most therapeutic attitude for physician and patient alike is one which regards illness, whatever its primary symptoms, as an opportunity for personal growth and change—and the physician as a catalyst and guide in this process. The treatments of choice at any level are therefore those which most effectively promote the individual's capacity for self-awareness and self-care.

My current practice resembles in

PHOTOGRAPH BY MARCELO MONTECINO

many ways my grandfather's of 60 years ago. I work with family members of all ages, singly and together, and consult about family problems and decisions as well as about acute and chronic illnesses. I make house calls when someone who needs me is too ill to come to my office. I rarely prescribe the powerful drugs that have been developed since my grandfather's practice—including the neuroleptics, antidepressants, and anxiolytics that are the staples of biological psychiatry—and still more rarely hospitalize my patients.

Many of those who come to me present with the kinds of problems that might bring them to any psychiatrist. But I am perhaps more likely than most to engage them actively in work on the physical and spiritual, as well as the psychological and interpersonal, aspects of these problems. I tend to see, and help my patients to see, that psychological problems are not simply indicators of underlying pathology. They are, often enough, signs that a new or renewed source of meaning and purpose in life are necessary.

Among the techniques I use—in addition to dynamic psychotherapy, Gestalt, guided imagery, and bioenergetics—I have found that periods of fasting (I must confess I have not resorted to the pineapple fast) can interrupt, or help a patient work through, a depressive or schizophrenic episode. I recommend exercise—everything from jogging and aerobic dancing to Tai Chi and yoga—trying to tailor the technique to the person. And I use acupuncture as well, which seems to relax patients, improve their moods, at least temporarily, and at times help them move through emotional blocks. During the treatment, depressed and affect-less people may dissolve in tears; repressed ones may feel surges of anger. Some rise from the acupuncture table with fresh insights: "I'm only staying sick," one depressed woman announced, "so I can make my husband take care of me."

Others present with long-standing serious physical problems. They come after receiving the most up-to-date and exhaustive work-ups—when they are about to take another plunge into psychotherapy, or undergo yet another series of diagnostic tests, another change in medication, or another surgical procedure. They come—I warn them in advance—prepared to take a fresh look at themselves, their illness, and its treatment.

A middle-aged woman, for example, presents with asthma and emphysema. Chronically dependent on steroids, inhalers, and emergency treatment with epinephrine, she's Cushing-oid, morbidly anxious, and suicidally depressed. Under my supervision, she changes her diet radically, substituting brown rice, vegetables, and fish for coffee and doughnuts, hamburgers and pizza. She sees some diminution in her pulmonary symptoms and begins to lose weight, which increases her feeling of self-sufficiency and encourages her to let me gradually reduce her medication. When acupuncture proves capable of aborting an acute asthmatic attack, she is willing to use acupressure at home to relieve attacks that previously might have brought her to the emergency room. The more she is able to take care of herself, the more willing she is to learn techniques she can use on her own. The better she feels, the more confident she becomes, the greater the improvement in her pulmonary functioning.

If holistic medicine has provided its proponents with a rallying point, it also offers us and our critics a challenge. We need to achieve a balance between openness to unconventional healers and regulation of unscrupulous practitioners who capitalize on the despair of prospective patients. There is nothing holistic about allowing poorly trained personnel to practice, condemning more traditional medical care, or claiming that diet, chiropractic, acupuncture, or homeopathy can cure every illness.

The diagnostic and therapeutic techniques that are increasingly widely used cry out for careful and sophisticated research. Even more important, we need to bring new methods, and indeed new attitudes, to the study of the approach to health care—call it holistic or not—that is evolving. Investigators will need to remember that established methods, such as the double-blind study, may be inappropriate for evaluating techniques which depend for their efficacy on the informed and active participation of patients.

The longer I practice, the less I am awed by the techniques themselves. I am increasingly aware of their utility as vehicles for the healing interaction between me and my patients. In the past we have too often factored this "placebo effect" out of our clinical investigations. We now need to take a thorough and critical look at this interaction, its development, and its biological as well as psychological consequences. We need to understand those factors which facilitate or frustrate the development of physicians who are able to establish a healing bond with their patients, and at the environments—emotional and physical, educational and social—in which physicians, other health-care workers, and patients may flourish.

In my own work, I am eager to create a setting for bringing together and putting to use what I have learned in mental hospitals, outpatient clinics, alternative mental health services, and my private "holistic" practice. I want to see if the holistic approach that has been developed among the well-to-do few can be extended to the masses of people, and determine if it offers an efficacious, cost-effective, and satisfying modification of conventional practice.

Whatever the outcome of these studies and efforts, I imagine the name "holistic medicine" will eventually be dropped, as it is ultimately a device of historical utility, not a necessity. Holistic medicine is not a new specialty. The name serves as a reminder of what is best and most enduring in medicine, and an opening into a new synthesis of contemporary biomedicine and the larger healing tradition of which it is but a part.

It is a way of approaching all health care, as useful and exciting for the surgeon and psychiatrist as for the family practitioner, as vital to practice in a tertiary care setting as in a rural retreat. It is, finally, an attitude of thoughtful openness to everything that may be useful in health care—to the healing techniques we may have ignored or disparaged, as well as those we learned in medical school and specialty training, to the healing power of the therapeutic encounter, to our patients' capacity to understand and care for themselves, and to our ability and need as physicians to grow and change. □

August Morning, Prince Edward Island. *A study in symmetry: heavy early morning dew and an energetic spider.*

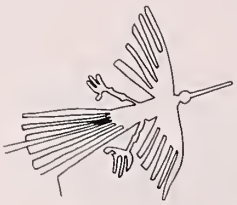
Three Photographs

by Gordon Scannell

Gordon Scannell '40 is editor of the Bulletin *and clinical professor of surgery at Massachusetts General Hospital.*

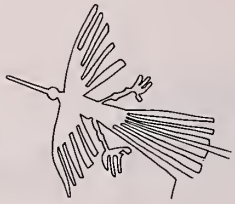
Woman of the Pyrenees. *On the Pilgrim Road to Santiago, we crossed the old Roman bridge over the Aragon, and drove 15 kilometers into the mountains to the small pueblo of Sinues, unchanged for centuries. In a village that seemed nearly deserted, we found this aged and ageless woman of Spain. She kindly opened the chapel for us. She was small, shrunken, her eyes red-rimmed, her smile friendly and tolerant.*

Paseo at Midday. *It is just after lunch in Calatayud, 100 kilometers or so from Madrid. The older men stroll away from us. They are the survivors. What they talk about I do not know; what they think I can only guess. They look like chromosomes. Walking briskly toward us are two young women of post-Franco Spain. It is spring.*



The Travel Program Of

Alumni Flights Abroad



This is a private travel program especially planned for the alumni of Harvard, Yale, Princeton and certain other distinguished universities. Designed for the educated and intelligent traveler, it is specifically planned for the person who might normally prefer to travel independently, visiting distant lands and regions where it is advantageous to travel as a group. The itineraries follow a carefully planned pace which offers a more comprehensive and rewarding manner of travel, and the programs include great civilizations, beautiful scenery and important sights in diverse and interesting portions of the world:

TREASURES OF ANTIQUITY: The treasures of classical antiquity in Greece and Asia Minor and the Aegean Isles, from the actual ruins of Troy and the capital of the Hittites at Hattusas to the great city-states such as Athens and Sparta and to cities conquered by Alexander the Great (16 to 38 days). *VALLEY OF THE NILE:* An unusually careful survey of ancient Egypt that unfolds the art, the history and the achievements of one of the most remarkable civilizations the world has ever known (19 days). *MEDITERRANEAN ODYSSEY:* The sites of antiquity in the western Mediterranean, from Carthage and the Roman cities of North Africa to the surprising ancient Greek ruins on the island of Sicily, together with the island of Malta (23 days).

EXPEDITION TO NEW GUINEA: The primitive stone-age culture of Papua-*New Guinea,* from the spectacular Highlands to the tribes of the Sepik River and the Karawari, as well as the Baining tribes on the island of New Britain (22 days). The *SOUTH PACIFIC:* a magnificent journey through the "down under" world of New Zealand and Australia, including the Southern Alps, the New Zealand Fiords, Tasmania, the Great Barrier Reef, the Australian Outback, and a host of other sights. 28 days, plus optional visits to South Seas islands such as Fiji and Tahiti.

INDIA, CENTRAL ASIA AND THE HIMALAYAS: The romantic world of the Moghul Empire and a far-reaching group of sights, ranging from the Khyber Pass and the Taj Mahal to lavish forts and palaces and the snow-capped Himalayas of Kashmir and Nepal (26 or 31 days). *SOUTH OF BOMBAY:* The unique and different world of south India and Sri Lanka (Ceylon) that offers ancient civilizations and works of art, palaces and celebrated temples, historic cities, and magnificent beaches and lush tropical lagoons and canals (23 or 31 days).

THE ORIENT: The serene beauty of ancient and modern Japan explored in depth, together with the classic sights and civilizations of southeast Asia (30 days). *BEYOND THE JAVA SEA:* A different perspective of Asia, from headhunter villages in the jungle of Borneo and Batak tribal villages in Sumatra to the ancient civilizations of Ceylon and the thousand-year-old temples of central Java (34 days).

EAST AFRICA AND THE SEYCHELLES: A superb program of safaris in the great wilderness areas of Kenya and Tanzania and with the beautiful scenery and unusual birds and vegetation of the islands of the Seychelles (14 to 32 days).

DISCOVERIES IN THE SOUTH: An unusual program that offers cruising among the islands of the Galapagos, the jungle of the Amazon, and astonishing ancient civilizations of the Andes and the southern desert of Peru (12 to 36 days), and *SOUTH AMERICA,* which covers the continent from the ancient sites and Spanish colonial cities of the Andes to Buenos Aires, the spectacular Iguassu Falls, Rio de Janeiro, and the futuristic city of Brasilia (23 days).

In addition to these far-reaching surveys, there is a special program entitled *"EUROPE REVISITED,"* which is designed to offer a new perspective for those who have already visited Europe in the past and who are already familiar with the major cities such as London, Paris and Rome. Included are medieval and Roman sites and the civilizations, cuisine and vineyards of *BURGUNDY AND PROVENCE*; medieval towns and cities, ancient abbeys in the Pyrenees and the astonishing prehistoric cave art of *SOUTHWEST FRANCE;* the heritage of *NORTHERN ITALY,* with Milan, Lake Como, Verona, Mantua, Vicenza, the villas of Palladio, Padua, Bologna, Ravenna and Venice; a survey of the works of Rembrandt, Rubens, Van Dyck, Vermeer, Brueghel and other old masters, together with historic towns and cities in *HOLLAND AND FLANDERS:* and a series of unusual journeys to the heritage of *WALES, SCOTLAND AND ENGLAND.*

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